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ORIGINAL CONTRIBUTIONS

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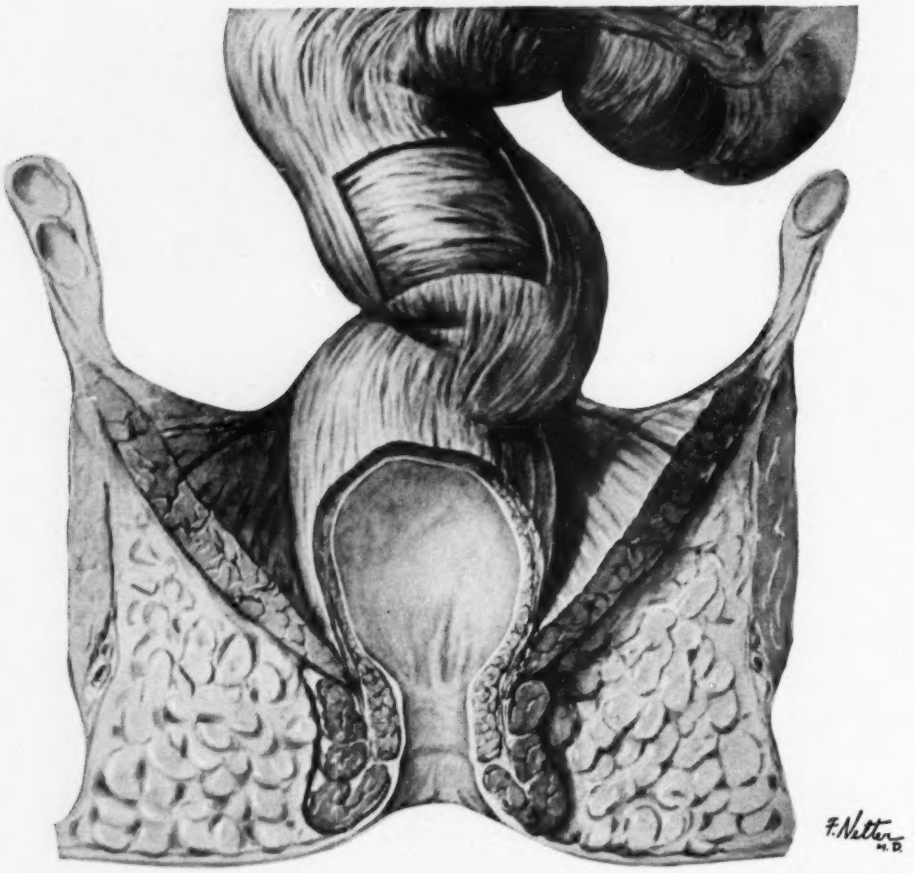

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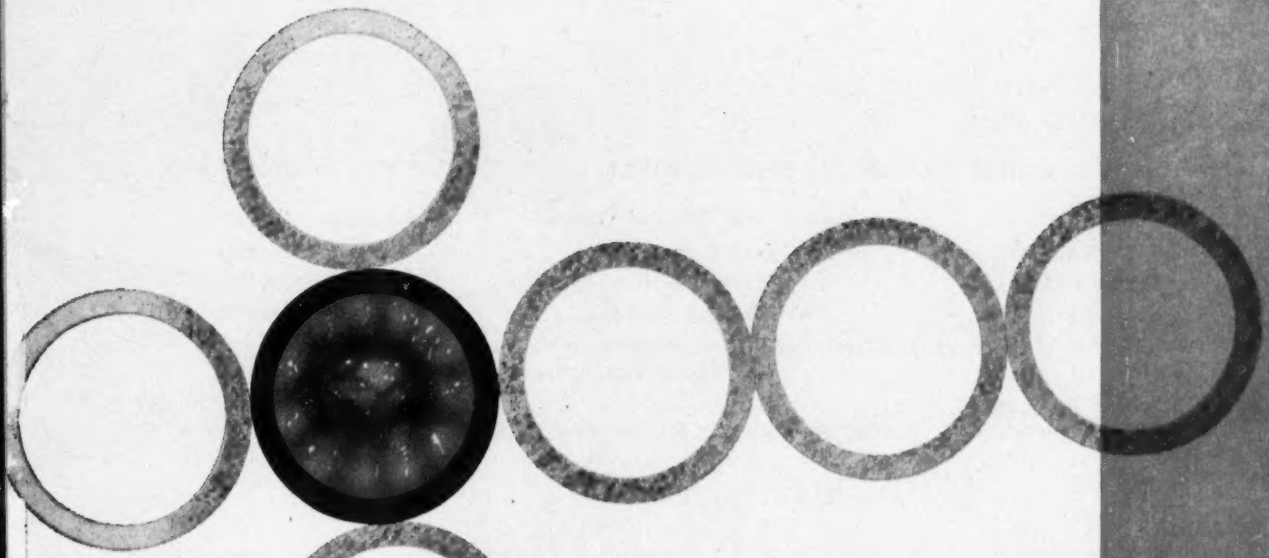

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1. Hoffmann, C. R.: Am. Pract. & Digest Treat. *4*:464, 1953.
2. Riese, J. A.: Am. J. Digest. Dis. *21*:81, 1954.

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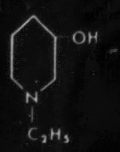

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1. ROGERS, W.P., AND GRAY, C.L.: AM. J. DIGEST. DIS. 19:180 (JUNE) 1952.

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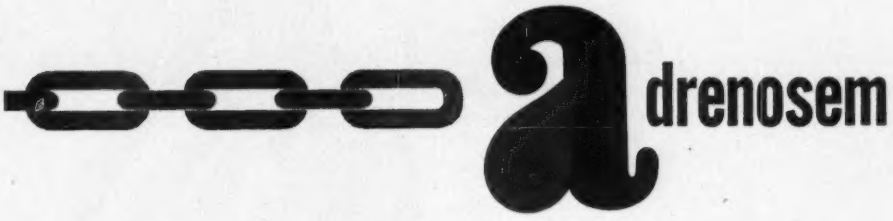
*Sherber, D. A.: The Control of Bleeding, Am. J. Surg. *86*:331 (Sept.) 1958.



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This low serum albumin concentration has been interpreted to reflect "a low protein intake as well as a retarded or failing support with protein released from protein reserves."[2] Unless the low level of serum albumin is corrected by enhanced protein nutrition, it "eventually means a low hemoglobin level and a low total red cell count with cells that have a normal color index."[2]

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1. Getz, H. R.; Westfall, I. S., and Henderson, H. J.: Nutrition in Tuberculosis as Evaluated by Blood Analysis, Am. Rev. Tuberc. *50*:96 (Aug.) 1944.
2. Getz, H. R.: Problems in Feeding the Tuberculous Patient, J. Am. Dietet. A. *30*:17 (Jan.) 1954.
3. Eichelberger, L., and McCluskey, K. L.: Chemical Studies in Tuberculosis: Plasma Proteins, Cholesterol and Corpuscle Volume, Arch. Int. Med. *40*:831 (Dec.) 1927.
4. Seibert, F. B.; Seibert, M. V.; Atno, A. J., and Campbell, H. W.: Variation in Protein and Polysaccharide Content of Sera in Chronic Diseases, Tuberculosis, Sarcoidosis, and Carcinoma, J. Clin. Invest. *26*:90 (Jan.) 1947.

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ANAPHYLACTOID INFLAMMATORY RESPONSES TO PREPARATIONS OF DUODENAL INTRINSIC FACTOR AND OF GASTRIC MUCIN

G. JASMIN, M.D.* AND H. SELYE, M.D., Ph.D., D.Sc., F.R.S. (C), Montreal, Canada
AND S. L. STEELMAN, Ph.D., Chicago Illinois.

IT HAD been observed (1) some time ago that, in rats given parenteral injections of egg-white, there develops a singular acute inflammatory reaction in certain predisposed "shock-organs," such as the snout, the ears, the paws and the genital region. Although histologically this response resembles certain hypergic inflammatory reactions, it is apparently not a true anaphylaxis, since it does not depend upon preliminary sensitization with the evocative agent. It has therefore been referred to as an "anaphylactoid inflammation." Subsequent investigations had shown that, in the crude egg-white, the ovomucoid fraction carries the activity (2), and that essentially similar responses can also be obtained with a variety of other substances, such as dextran, hyaluronidase, polyvinylpyrrolidone-globin, etc. (3, 4, 5). The reaction has aroused a great deal of interest in recent years, especially because it proved to be readily inhibited by anti-inflammatory hormones (ACTH, cortisone, cortisol) and various antihistaminics. Conversely, it is aggravated by adrenalectomy (presumably through the suppression of endogenous antiphlogistic corticoid secretion) and by treatment with prophlogistic hormones, such as desoxycorticosterone or somatotrophic hormone. The rather voluminous literature dealing with this singular phenomenon need not be discussed here, since it has been extensively reviewed in a series of publications (5, 6, 7, 8, 9).

The object of this communication is to report upon the production of anaphylactoid inflammation by preparations of duodenal intrinsic factor and of gastric mucin, in intact and in adrenalectomized rats.

MATERIALS

Experimental animals.—In all these experiments, we used male Sprague-Dawley rats, weighing 130-140 gm. and maintained on Purina Fox Chow. They received tap water to drink, except in those experiments in which one group was adrenalectomized; here, both the intact and the adrenal-deficient animals were given 1% NaCl as a drinking fluid, for uniformity's sake, although only the latter actually required salt supplements for maintenance.

Adrenalectomy.—In all those groups in which we wished to examine the effect of adrenal-insufficiency, the suprarenals were removed through two dorsal subcostal incisions, 48 hours prior to the test.

Institute of Experimental Medicine and Surgery, Université de Montréal, Montreal, Canada (G. Jasmin, H. Selye) —Biochemical Research Department, The Armour Laboratories, Chicago, Illinois (S. L. Steelman).

These experiments were performed with the aid of a grant from the Ministère de la Santé de la Province de Québec.

The authors are also indebted to Miss Lise Farley for technical assistance, and to Mr. Kai Nielsen for the microphotographs.

*Fellow of the Canadian Life Insurance Officers Association.

Materials for the production of the anaphylactoid inflammation.—Two gastro-intestinal preparations known to be rich in muco-proteins were employed. The first was Armour's duodenal intrinsic factor (preparation No. 207), which contains 52% protein, 28% non-dialyzable solids, 72% dialyzable solids and 320γ/gm. of vitamin B_{12}-Binding Capacity. The second was a partially purified gastric mucin preparation, made by the Fine Laboratories. Both these extracts were injected under light ether anesthesia, into the jugular vein. Invariably, aqueous solutions were given, at the concentrations indicated in our Tables (cf. Tables I, II and III). The total dose was always 1 ml. in the case of the intrinsic factor and 2 ml. in the case of the gastric mucin preparation.

Assessment of the response.—The anaphylactoid inflammation obtained was appraised in a scale ranging between 0 to +++, as judged by the degree of edema observed in the paws, snout, ears and genital region. In our Tables, only the means are given, but in general, the reactions were fairly consistent in the various individuals of any one group.

It should be especially mentioned that, in order to obtain maximal reactions, the dose of the irritant must remain within a certain optimal range, since small amounts are ineffective, and excessive quantities tend to cause shock, which interferes with the exudative inflammatory response. All doses used in this study were within this effective range and caused no evidence of shock.

Autopsy performed at the end of each experiment showed slight hyperemia of the abdominal organs, but no other visible signs of damage.

RESULTS

Experiments with duodenal intrinsic factor.—In the first experiment, anaphylactoid inflammation was produced in normal rats, treated with various concentrations of duodenal intrinsic factor, as outlined in Table I.

TABLE I

ANAPHYLACTOID INFLAMMATION IN NORMAL RATS TREATED WITH VARIOUS CONCENTRATIONS OF DUODENAL INTRINSIC FACTOR

Group	No. of animals	Concentration	Response	
			After 1 hr.	After 2 hrs.
I	6	10%	+++	++
II	6	5%	+	0
III	6	1%	0	0

It will be noted that a 10% solution of duodenal intrinsic factor produced a marked anaphylactoid inflammation after one hour, which was still quite obvious after two hours. A 5% solution elicited only a transient and mild reaction, while a 1% solution proved to be ineffective.

In the second experiment, we compared the response to a 5% solution of duodenal intrinsic factor, in normal and in adrenalectomized animals, as outlined in Table II.

TABLE II

ANAPHYLACTOID INFLAMMATION IN NORMAL AND ADRENALECTOMIZED RATS TREATED WITH DUODENAL INTRINSIC FACTOR

Group	No. of animals	Concentration	Response After 1 hr.	Response After 2 hrs.
I Normal	6	5%	+	0
II Adrenalectomized	6	5%	+++	++

It will be noted that here again the normal rats responded only with a mild and transient reaction. On the other hand, the adrenalectomized animals exhibited a very pronounced and more persistent response. This confirms, for the agent employed here, that suprarenalectomy sensitizes to this type of anaphylactoid response.

Experiment with gastric mucin.—In the third experiment, the effect of a 3% solution of gastric mucin was compared in normal and adrenalectomized rats. The preparation available to us was not readily soluble in water. Hence, a saturated solution was prepared and, after separation of the supernatant fluid from the sediment (by centrifugation), only the former was injected. Its concentration was determined by lyophilization and weighing of the dry residue, which proved to represent 3% of the total. Our results are given in Table III.

TABLE III

ANAPHYLACTOID INFLAMMATION IN NORMAL AND ADRENALECTOMIZED RATS TREATED WITH GASTRIC MUCIN

Group	No. of animals	Concentration	Response After 1 hr.	Response After 2 hrs.
I Normal	10	3%	++	+
II Adrenalectomized	10	3%	++	++

In this case, the difference between normal and adrenalectomized animals was less pronounced, since both groups responded with a subnormal and yet quite evident reaction. Nevertheless, the reaction proved to be more persistent in the adrenalectomized than in the intact rats.

Histologic examination of the paws showed that the response corresponds to a typical serous inflammation, such as is usually obtained with any among the agents eliciting the "anaphylactoid response." This is illustrated by the adjacent photographs.

SUMMARY AND CONCLUSIONS

Experiments on rats showed that intravenously administered, partially purified, preparations of duodenal intrinsic factor and of gastric mucin are capable of producing a typical anaphylactoid inflammation in the rat.

This response was more pronounced in adrenalectomized than in intact control animals.

Since the preparations were not completely homogenous, our experiments do not exclude the possibility that the inflammatory response could have been produced, wholly or in part, by contaminating

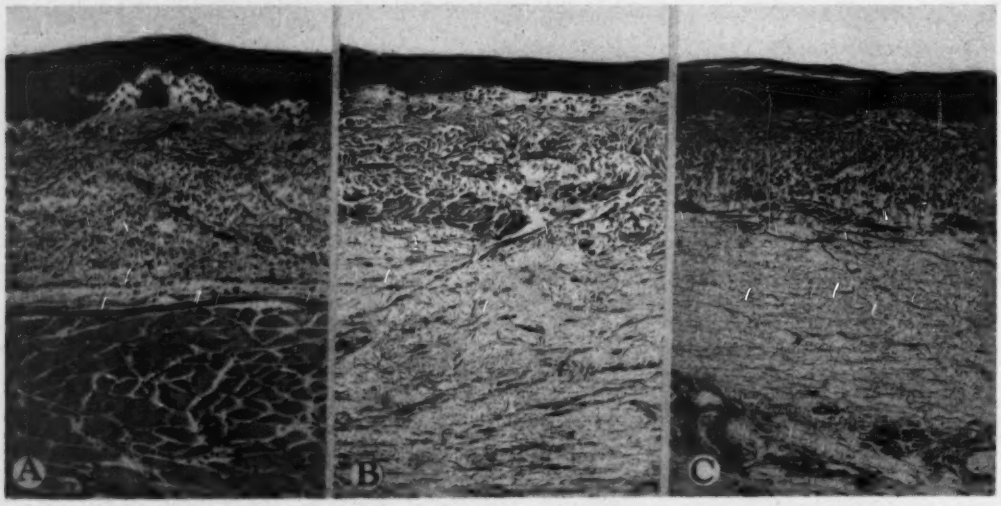

Fig. 1: HISTOLOGIC ASPECT OF THE SUBCUTANEOUS TISSUE UNDERNEATH THE EPIDERMIS ON THE DORSAL SURFACE OF THE HIND PAW.—Compare the normal aspect of the loose connective tissue (A) with the intensely edematous connective tissue just underneath the derma of the rat which had been treated with the intrinsic duodenal preparation (B) or with gastric mucin (C). Cellular infiltration is minimal in both the treated animals.

substances rather than by the intrinsic factor and the mucin themselves. It is evident, however, that a characteristic anaphylactoid inflammation can be elicited by products of the gastro-intestinal tract.

REFERENCES

1. Selye, H.: "Studies on Adaptation." Endocrinology, *21*:169 (1937).
2. Leger, J. and Masson, G.: "Studies on egg white sensitivity in the rat." Ann. Allergy, *6*:131 (1948).
3. Voorhees, A. B., Baker, H. J. and Pulaski, E. J.: "Reactions of albino rats to dextran." Proc. Soc. Exper. Biol. & Med. *76*:254 (1951).
4. Swingle, W. W., Fedor, E. J., Maxwell, R., Den, M. and Barlow, G.: "Cortisone foretreatment of adrenalectomized rats infused with globin and dextran." Am. J. Physiol. *172*:534 (1953).
5. Halpern, B. N.: "Histamine, antihistaminiques de synthèse et processus inflammatoires," in: The Mechanism of Inflammation. An International Symposium, Ed.: G. Jasmin and A. Robert, Montreal, Acta Inc., Medical Publishers (1953).
6. Selye, H.: Stress. The Physiology and Pathology of Exposure to Stress, Montreal, Acta Inc., Medical Publishers (1950).
7. Selye, H.: First Annual Report on Stress, Montreal, Acta Inc., Medical Publishers (1951).
8. Selye, H. and Horava, A.: Second Annual Report on Stress, Montreal, Acta Inc., Medical Publishers (1952).
9. Selye, H. and Horava, A.: Third Annual Report on Stress, Montreal, Acta Inc., Medical Publishers (1953).

VISUALIZATION OF THE BILIARY TRACT BY MEANS OF BILIGRAFIN, ESPECIALLY AFTER CHOLECYSTECTOMY

WERNER TESCHENDORF, M. D., Cologne, Germany.

THE CLINICAL procedure of cholangiography is only possible where surgical intervention is carried out. Laparoscopic cholangiography is only undertaken by the expert in this field and only in the presence of special indications. Besides, success cannot always be guaranteed with it. Otherwise, cholangiography is limited to fistula cases.

Biliary tract visualization following administration of egg-yolk for the purpose of testing the visualization of a filled gall-bladder, provoked by stimulation to evacuate same, does not rank as a method properly speaking. In a great number of gallstone cases the evacuation test cannot be used. At best, the cystic and bile ducts are seen; so too the hepatic duct, but only when the valvular mechanism does not operate. Even if Telepaque, excellently tolerated and especially well visualized in the biliary tract, is used, a regular visualization of the biliary tract is not obtained. This drawback renders Telepaque unsuitable in making differential diagnoses. The procedure of visualizing biliary passages is not carried out after cholecystectomy. A demonstration of same, however, is possible with "Biligrafin," a new preparation offered now by Schering A. G. Berlin. This preparation differs chemically from others in common use in the following manner:

Priodax = Biliselectan-$^{\beta}$-(oxy-3,5-diiodophenyl-$^{\alpha}$-phenyl-propionic acid.

Telepaque = $^{\beta}$-(3-amino-2,4,6-triiodophenyl)-$^{\alpha}$-ethyl-propionic acid.

Teridax = $^{\alpha}$-ethyl-$^{\beta}$-(2,4,6-triiodo-3-hydroxy-phenyl)-propionic acid.

Biligrafin = N,N'-adipin-di-(3-amino-2,4,6-triiodo) benzoic acid.

In cholecystography Biligrafin is given intravenously. It leads to visualization of the biliary tract only when, instead of a 1 x 20 c.c. ampoule, 2 x 20 cc. ampoules are used. The latter dose of 40 c.c. is easily tolerated.

Biligrafin is the substance referred to in an editorial by Dr. Franz J. Lust in the February 1954 issue of this journal.

The firm of Schering A. G. Berlin made available to us another preparation, i.e., a 40% compound of an iodolithium salt, known by us as "Biligrafin forte."

The data to follow deal chiefly with this preparation, which has not been put as yet on the market, for other centers have disclosed that following trials with it, malaise and even states of collapse have followed its injection.

Our investigations cover 250 cases, 200 of whom have been given "Biligrafin forte."

No evidence of intolerance has been noted by us. In one case there developed a transient condition verging on shock but apparently not associated with any degree of risk. In addition, we have administered the preparation to 15 cases of icterus and subicterus; yet nothing special was observed after the injection, nor was there any intensification of the jaundice.

We should like to stress, however, that the reaction of the patient is essentially dependent on the mode of injection adopted. The length of time taken to inject 20 c.c. of a 40% solution (or 40 c.c. of a 20% solution) of "Biligrafin forte" mentioned above must therefore not fall short of 8 minutes. After injecting half of the solution, a pause of 1-2 minutes is recommended.

The firm supplies sample ampoules for testing purposes, so that the degree to which the preparation is tolerated can be assessed. However, any reactions only occur following injection of larger quantities. For this reason, injection at a slow rate and marked possibly with a pause of 1-2 minutes is to be recommended in preference to a test dose given beforehand. The risk of iodine hypersensitivity does not really arise because iodine is seemingly bound firmly in the molecule and does not become split off. Provided these precautions were not neglected, the two preparations tested by us were found to be perfectly tolerated, apart from the one case mentioned already where there had been a mild reaction, to which no importance could be attached.

Fig. 1

Cholecystectomy. Residual stones in common duct.

The pictures were taken preferably 10, 20, 30 and 40 minutes after the injection.

The Biligrafin for intravenous injection possesses the following advantages:

1. The gall-bladder is visualized. So too usually are any stones not detectable with the aid of other preparations used in cholecystography. However, space does not permit a discussion on roentgen examinations of this kind.

2. The second advantage of this method is the possibility of visualizing the biliary tract perfectly clearly. This held good for 98% of our cases. The preparation is therefore ideal for follow-up examinations after operations. For this reason, we avoided duplicate examinations, whereby oral administration revealed stones in the gall-bladder, in favour of pre-operative Biligrafin examination, which showed, in addition, any stones that might have formed in the biliary tract. For this reason, our radiographs to be shown hereunder were confined to cholecystectomized patients; in these Biligrafin revealed stones and other changes in the biliary system.

Fig. 1 shows the biliary tract of a patient 7 months after she was cholecystectomized. She was still complaining of colic. The bile ducts are found to be dilated. There is a bulge in the outline of the common bile duct due to stone formation. It is for this reason that the bile duct does not convey the usual impression of narrowing down to the point. The follow-up examination with Biligrafin in this case reveals the presence of a stone missed at operation.

In Fig. 2a, only the bile ducts are visualized. The original pictures revealed a small shrunken gall-bladder dimly outlined in the present picture. We see in this case a marked dilatation of the bile duct system. The hepatic duct, much thickened, is observed to pursue a tortuous course. The cystic duct is represented as a rounded bulge. The upper part of the bile duct is kinked. The duct itself contains 2 stones.

Fig. 2b is taken from the same patient following cholecystectomy and removal of the stones from the

Fig. 2a

Cholecystitis, shrinkage of gall-bladder, obstruction in the hepatic duct. 2 stones in the common duct.

Fig. 2b

The same patient as in Fig. 2a. Cholecystectomy with removal of the stone in the common duct. Biliary tract still dilated.

Fig. 3

Cholecystectomy 1943. Stones in the stump of the cystic duct.

Fig. 5

Cholecystectomy 15 years ago. Common bile duct stone. Dilatation of the cystic duct stump.

bile duct. The operation has failed to abolish the widening of the hepatic and kinking of the common bile ducts.

Fig. 3 is taken from a patient, who still complains, despite cholecystectomy in 1943. Our examination revealed that she had dilatation of the cystic duct which was seen to contain a stone at its lower pole.

In Fig. 4a only the biliary tract is seen, and Biliselectan and Biligrafin fail to bring out the outline of the gall-bladder. After Biligrafin, the hepatic and common bile ducts but not the cystic duct were rendered well visible. In all pictures we noticed a shadow at a point along the course of the cystic duct. The shadow we presumed to be a stone. This was confirmed at operation.

Fig. 4b is taken from the same patient following operation. The stone is no longer to be seen. The bile

Fig. 4a

Occlusion of the cystic duct by a stone.

Fig. 4b

Same case as in Fig. 4a, but after removal of gall-bladder and the stones in the cystic duct. Normal biliary tract.

duct system now empties in a normal manner. At the same time of the examination the patient had absolutely no complaints to make. Moreover, after cholecystectomy the stump of the cystic duct is visible. This picture therefore serves, in addition, to demonstrate normal biliary passages following cholecystectomy.

Fig. 5 comes from a patient cholecystectomized 15 years ago. For the last two to three years, symptoms have returned with genuinely colicky pain in recent months. The roentgen picture shows greatly dilated ducts. In the bile duct two rather large cholesterin stones are seen. The stump of the cystic duct is dilated to such an extent that the possibility of regeneration of the gall-bladder has to be considered. In order to exclude the possibility that this shadow is the result of regurgitation of Biligrafin from the duodenal cap, we filled the stomach with contrast barium. It was found that the duodenal cap and the rounded shadow were not identical, but that the latter was really the stump of a dilated cystic duct.

Fig. 6 illustrates a source of error. The rounded shadow which lies below an air bubble is not that of a regenerated gall-bladder. The patient had been cholecystectomized 5 years ago. The bile duct system is free from any obstructions. Hepatic and common bile ducts can be seen. The rounded shadow is that of the duodenal cap, which has become refilled as the result of regurgitation via the papilla Vateri into the duodenum. Biligrafin can collect in the duodenum in amounts so great that the latter is rendered visible. Filling the stomach with contrast barium determines the ultimate decision regarding the source of the shadow.

The examples just mentioned illustrate a method which provides a perfectly satisfactory way of examining the biliary tract even in cholecystectomized cases. The fundamental cause of post-operative complaints can, in this way, be more easily ascertained. Moreover, the recurrence of stone, or the presence of stones undetected earlier at operation, can be established. Kinks and other changes in the ducts are also revealed by this method. Of the greatest importance is confirmation that the biliary system appears normal in outline and is devoid of stones; for then the investigation of other organs can be taken up in the search for the cause of post-operative complaints. In many such cases we discovered peptic ulcer or renal pathology showing symptoms wrongly ascribed post-operatively to the gall-bladder.

Fig. 6

Absence of gall-bladder shadow. Regurgitation of Biligrafin into the duodenal cap.

Biligrafin does not rule out the use of oral cholecystography. Of course, the oral route is of no avail in cholecystectomized patients. In all other cases, we carry out an earlier examination with Priodax or Telepaque. If stones are found in the gall-bladder the visualization of the biliary tract with Biligrafin provides a thoroughly trustworthy answer, whether or not the biliary tract contains stones. The importance of this pre-operative procedure needs no further stress. When the gall-bladder fails to fill, the possibility of hepatic insufficiency has to be considered. In such cases, a shadow of the renal pelvis is observed, because then the kidneys have the task of excreting the contrast substance.

Although we have never observed an aggravation of conditions in liver insufficiency as a result of Biligrafin, we should like to emphasize, however, that we did not consider the use of Biligrafin indicated in clinically established cases of liver insufficiency; for this reason we have not attempted to examine these patients with Biligrafin. We cannot, in the course of this article, go more deeply into this matter; for we wish to confine attention to visualization of the biliary tract post-operatively. It was possible to consider this aspect in connection with the examples just given.

SUMMARY

Cholangiography with Biligrafin permits visualization of the biliary tract. Radiographs are taken 10, 20, 30 and 40 minutes after the injection. The hepatic and common bile ducts are visualized in 98% of cases. Moreover, the stump of the cystic ducts is seen in most cases. In this way, post-operative complaints are very often traced back to their origins. This article dealt chiefly with the visualization of the biliary tract in cholecystectomized patients.

BIBLIOGRAPHY

Bernhard, Fr.: Die Bedeutung der Cholangiographie für Praxis und Forschung. Chirurg 9 (1937):201.
Der Sperrmechanismus im Ductus hepaticus und seine Bedeutung für die Gallenabsonderung sowie für die Behandlung der Gallenwegserkrankungen.

Benassi, E.: La Colangiocistografia con Biligrafin. Radiologia 9 (1953):795.

Billion, H.: Vergleichende Untersuchungen mit radioaktivem Biliselektan und Biligrafin. Erscheint im Kongressheft des Deutschen Medizin. Journals.

Conde Otero, Franzisco and Eiber, Enrique: Colecistocolangiogramas; obtenidos por ingestion del colorante. Arch. Hosp. Universitario, Habana, Nov.-Dec., 1952, 4, 691-709. Roentgenology 70 (1953):650.

Frommhold, W.: Ein neuartiges Kontrastmittel für intravenöse Cholecystographie. Fortschr. Röntgenstr. 79 (1953): 283.
Entwicklung und Fortschritte der Cholecystographie und Cholangiographie. Berliner Gesundheitsblatt, Heft 22 (1953).

Gaebel, E und Teschendorf, W.: Darstellung der Gallenwege mit Biligrafin (Schering) (unblutige Cholangiographie). Röntgen-Blätter 4 (1953):162.
Über Fortschritte in der röntgenologischen Darstellung der Gallenblase. Fortschr. der Röntgenstrahlen 81, (1954).

Hornykiewytsch, Th. und Stender, H. St.: Intravenöse Cholangiopraphie. Fortschr. Röntgenstr—79 (1953):292.

Langecker, H., Harwart, A. und Junkmann, K.: 2,4,6,-Trijod-3-acetaminobenzoesäure-Abkömmlinge als Kontrastmittel. Arch. exper. Path. u. Pharmakol, Bd. 220 (1953), S.195.

Lust, F. J.: The roentgenological demonstration of the gallbladder and bile ducts by intravenous injection of NN-ADIPIN-DI-(3 AMINO-2,4,6-TRI-IODO-BENZOIC ACID). Amer. J. Digest. Dis., 21 (1954):60.

Nemours, Auguste et Barag, N.: La cholangiocholecystographie intraveneuse opacification des voies biliaires intra-et extrahepatic par une nouvelle substance Presse Med. 61 (1953):61.

Pahl, R.: Schnelle und erweiterte Gallenwegsdiagnostik mit dem neuen i.v. applizierbaren. Kontarstmittel "Biligrafin." D. med. Wschr. 79 (1954):363.

Schilling, C.: Bisherige Untersuchungsergebnisse mit dem neuen Kontrastmittel SH 216 zur Darstellung des Gallenwegsystems. Fortschr. Röntgenstr. 80 (1954):490.

Sénèque, J., Le Canuet, R., Debray, Ch., Roux, M. et Aussage, J.: La cholangiographie par voie veineuse. Sa place dans l'exploration radiologiques des voies biliaires. Presse Med. 14 (1954):281.

GASTRODUODENAL TISSUE EXTRACTS IN THE TREATMENT OF PEPTIC ULCER WITH SPECIAL REFERENCE TO THE EFFECTIVENESS OF ROBUDEN

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A NEW approach in the therapy of peptic ulcer was inaugurated in 1925 with the publication by Rivers (1) of his results in the treatment of fifty peptic ulcer patients with an extract of duodenal mucosa, eight having benefited materially. Animal experiments followed, and in 1937 Stalker and his associates (2) reported some benefit from the use of 10 gm. duodenal extract daily in protecting cinchophen dogs from developing ulcers. In the same year success was also reported in preventing the development of cinchophen ulcers in dogs by feeding them half-a-pound of hog stomach and duodenum preparation daily (3).

The anti-ulcer activity of the gastrointestinal preparations was at the time attributed to enterogastrone, which was defined as "the specific material which is present in the upper intestinal mucosa and is responsible physiologically for the inhibition of gastric secretion and motility which occurs when an adequate concentration of fat or sugar is present in the lumen of the upper intestine" (4, 5).

The view that the anti-ulcer activity of gastrointestinal extracts was due to the anti-secretory principle was subsequently shown to be erroneous, but unfortunately, in the meantime, the designation "enterogastrone" had been applied to many types of intestinal extracts with little or no reference to their anti-ulcer or anti-secretory activity. Confusion in the terminology was further increased with the discovery that extracts of urine also protect against experimental ulcers (6, 7, 8) and depressed gastric secretion (9, 10, 11, 12).

The terminology employed in this publication is that advocated by Grossman (13) and by Friedman (14). The substances under consideration are defined as follows: *enterogastrone* is the gastric secretory depressant obtained from intestinal extracts. A corresponding gastric secretory depressant can be extracted from urine and is referred to as *urogastrone*. The effective principle present in tissue extracts and obtainable from urine, prevents the development of experimental ulcers and promotes epithelialization and tissue proliferation at the ulcer site and is designated *anthelone* (15). Friedman (16) has made two well-founded suggestions which help to clarify the situation further: that the various "extracts" obtained from the intestine and from the urine should be considered as concentrates of intestinal or urinary origin, and that until proof is available that the exogenous agent of an organ extract is identical with the endogenous agent elaborated by that organ *in situ*, it would be desirable to regard the effects of the organ extract as "pharmacologic" rather than "physiologic" (17).

Ivy and his co-workers reported in 1941 on the effect of crude extracts of hog's upper intestinal mucosa on the ulcer disease in Mann-Williamson dogs (18) and in 1945 (19) they reported on the inhibitory effect of the oral administration of such preparations in M-W dogs. Somewhat later they discussed favourably the effect of parenteral administration of a refined gastric and upper-intestinal extract ("enterogastrone") in 58 patients (20). While their results were encouragingly good, the authors stated that this form of treatment could do no more than the standard diet-antacid regime, and that it was indicated only in patients who fail to respond to such treatment, who have no organic obstruction at the pylorus and who refuse needed surgical therapy. The authors considered the relative absence of recurrences and the reported evidence of radiologic improvement encouraging.

Sandweiss (21) and Pollard (22) found "enterogastrone concentrates" to be ineffective in preventing recurrences of ulcer in man. Wollum and Pollard (23) recorded similar findings, stating in addition that

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prolonged administration of oral "enterogastrone" in a dosage of 16 grams daily, or intramuscularly in a dosage of 200 mg. six times weekly did not significantly alter the rate of gastric secretion, the free hydrochloric acid or pepsin content of the gastric juice in these patients. Used in this way, "enterogastrone" failed to influence favourably the clinical course in 76% of 34 patients with severe chronic peptic ulcer, or to alter significantly the gastric secretory pattern or the gastric motility. Kirsner and his associates (24) studied the nocturnal and twenty-four hour secretions under the influence of "enterogastrone" administered intragluteally in five doses daily, ranging in total daily dose from 100 to 300 mg. The aspirations were started immediately after the last injection. The results were variable and somewhat unpredictable. While large amounts appeared to be increasingly effective, the inhibition was not consistently related to the dosage, very large amounts sometimes being ineffective, while moderate quantities often reduced the secretion markedly. In another publication the same authors also reported that intramuscular injections of "enterogastrone" did not conclusively influence the secretory response to insulin and histamine stimulation. Wirts and Friedman (25) failed to influence favourably the ulcer symptoms in 38 patients treated with large oral doses of crude enterogastrone-like concentrates. At the end of a year of such therapy the results were similar in the concentrate-treated group and in a group of ulcer patients receiving a placebo. In studies on 10 volunteers, Ferayorni and his collaborators (26) found that 200 mg. "enterogastrone" administered intramuscularly did not significantly affect the gastric secretory response to histamine during a double histamine test. Administered in doses up to 400 mg. intramuscularly and 18 gm. orally also failed to affect significantly the gastric secretory response to a modified Ewald test meal. Similarly disappointing results were reported by Bone and his associates (27), who divided 36 patients, 33 of whom had X-Ray evidence of peptic ulcer, into two groups, treating one group with "enterogastrone," the other with crude liver extract indistinguishable in appearance from "enterogastrone." Both were administered intramuscularly, the "enterogastrone" in 200 mg. doses. There was no significant difference in the results obtained in the two groups, slightly over half of the patients in each group improving during the treatment and lapsing into the pretreatment state on termination of the treatment. There was no significant difference in the X-Ray findings, volume secretion and gastric acidity in the "enterogastrone" and control groups.

Results similar to those obtained with intestinal extracts have been reported with urinary extracts. A substance with anti-secretory properties, urogastrone, was identified in the urine of healthy subjects (28) as well as in that of ulcer patients (29) though possibly in somewhat smaller concentration in the latter (16). The anti-ulcer effects of urine extracts, believed to be due to urinary anthelone, were demonstrated experimentally (29, 30, 31) in dogs subjected to the ulcerogenic operation of duodenal drainage by the Mann-Williamson technique. The absence of anthelone in the urine of duodenal ulcer patients (8) tends to support the view that peptic ulcer in man may be due to the deficiency of a factor, probably enteric in origin, which normally protects the individual against the development of peptic ulcer. There has so far not been any explanation advanced as to why this deficiency should be present in some individuals and not in others.

Efforts have also been made to influence the course of ulcerative colitis with an extract prepared from hog intestine. Gill (32) reported marked symptomatic relief in seven of ten patients following treatment with a powdered preparation of hog duodenum for a period of one month. Exacerbations and remissions coincided with withdrawal and readministration of the preparation. The cycle was repeated several times in two of the patients. In a second publication, he reported continuation of good results. Similarly good results were reported by others (30, 33).

Coincidentally with, and independently of the American efforts directed toward the extraction of a peptic-ulcer-healing substance from the gastrointestinal mucosa, which culminated in the preparation of "enterogastrone," and in the isolation from the urine of a related substance, anthelone, Swiss investigators working along similar lines since 1937, have elaborated an extract which they have named Robuden. The extract is prepared from the mucosa and muscularis of the stomach and small intestine of freshly slaughtered hogs. While the exact method of preparation is not described, it is emphasized that the extract is protein-free. A water-soluble fraction is processed for intramuscular injection, there being one for the treatment of gastric ulcer and another for the treatment of duodenal ulcer, the respective extracts containing a preponderance of material from the stomach, for the treatment of gastric ulcer, and from the duodenum for the treatment of duodenal ulcer.

This substance is said to possess mucosa-protecting properties and probably also a regenerative, proliferative and vascularization-promoting action, the latter being effective in the entire depth of the gastrointestinal wall.

The water-soluble, injectable material has been reported (31) to have no effect on the gastric secretion provoked by histamine or insulin. In this respect, as well as in its chemical characteristics, it differs from "enterogastrone" preparations available commercially.

Schmassmann (23) points out that the attempts to treat peptic ulcer with extracts made from the wall of the gastrointestinal tract are based on the supposition that one or more hormone-like substances, responsible (perhaps independently of sympathetic or parasympathetic mechanisms) for the normal functioning of the upper gastrointestinal tract with respect to motility and secretion, is or are produced in the wall of the gastrointestinal tract. The nature of such extracts was also considered in the American literature (22, 35, 36). The principle of treating with protective substances must be considered in the nature of substitution therapy, states Burghartz (37), who also believes that Robuden is not identical with the so-called "enterogastrone" extracts.

Significant support for the efficacy of the Swiss preparations is reported in a number of publications. Roulet produced peptic ulceration in guinea pigs

(proved by laparotomy) by means of daily subcutaneous injections of histamine. Healing of such ulcers was achieved with Robuden therapy even if the histamine injections were continued during the treatment (38, 39). The ulcers were produced in the experimental animals without difficulty by employing a method described by Roulet (38) and by Vallery-Radot and his associates (40). Roulet concludes that Robuden has a beneficial effect on the healing of these ulcers, both as indicated in the gross evidence of healing and in the microscopic evidence of arrest of progress at the margins of the ulcers (sharper demarcation) and the increase in granulation tissue in the base of the ulcer. An interesting observation, which must await confirmation, deals with the apparent ability of Robuden to influence favourably the capacity of gastric mucus to adsorb histamine-like substances and pepsin, which capacity, these authors maintain, is considerably reduced in peptic ulcer patients (41, 42).

With one dissenting report (43), clinical results, as recorded in the literature are essentially favourable. Most of the observers report control of symptoms after three to eight injections in a fairly large percentage of treated patients: Herzog 52% (44); Surkes 64% (45); Schmassmann 79% (46); Neumann 80% (47) in gastric ulcer patients; and in duodenal ulcer patients: Schmassmann 43% (46) and Surkes 81% (45).

Burghartz (37), in discussing the possible relationship between Robuden and "enterogastrone," states that these, as well as "urogastrone," must be considered a form of substitution therapy; he also emphasizes the difficulty of precise evaluation of therapeutic success. His first series consisted of 103 patients who were treated with Robuden to the exclusion of all other forms of therapy. Of these 59 were ambulatory and 44 were hospitalized. There were 44 gastric, 51 duodenal and 1 jejunal ulcers. Two of the patients developed allergic manifestations during the course of therapy (fever, chills, rhinitis and evidence of irritation at the site of the injection). All other patients became symptom-free in an average of seven to eight days, and healing was established to have occurred within an average of five weeks. His series has since been increased to 277, the results being published in 1951 (48).

Thus it may be seen from the American and European literature that various preparations of gastrointestinal tissue have definite anti-secretory and anti-ulcer effects. These are probably due to two distinct principles, namely "enterogastrone" and enteric anthelone respectively. Preparations showing marked "enterogastrone" activity have shown little beneficial effect in human peptic ulcer. It is probable that commercial "enterogastrone concentrates" failed in anti-ulcer activity in man because of absence or near-absence of anthelone in this preparation. Gastrointestinal preparations are, however, available which have a distinct anti-ulcer activity without having anti-secretory power. The commercial preparation Robuden, which has been employed in the present study, and which is the subject of several favourable reports from European centers, probably owes its anti-ulcer activity to a high content of anthelone (49).

The inherent difference between Robuden and "enterogastrone," and the encouraging European results with the former preparation were of sufficient interest to warrant a clinical trial.

METHODS

The pitfalls incident to the evaluation of the results of any therapeutic method were recognized and therefore considerable thought was given to the question of controls and to the selection of "cases" for study. The standard method of treating one group of patients with the preparation under study and another equivalent group with a placebo, was considered and discarded. The validity of such comparative studies on a relatively small group must depend on the selection, for the two groups, of patients of comparable age, location of the lesion, severity and duration of the disease, the economic status of the patient, the emotional stresses to which he is subjected in his daily life, as well as other, imponderable factors. The selection of such pairs of even approximately comparable patients is a well-nigh impossible task; to use two numerically equal groups, without regard to these factors, cannot be considered a controlled study. The utilization of each patient as his own control was decided upon as an adequately reliable method of evaluating the effect of therapy in this study.

The selection of patients for this investigation was based upon a) relatively long duration of the illness, and b) the lack of satisfactory results in spite of consistent trial over an adequately long period of time with at least one, but preferably more than one form of therapy. All but two were known to have been suffering from peptic ulcer for periods ranging from 5 to 30 years, with the exception of cases 7 and 12 who had had peptic ulcer for two years. All but these two patients had been under the care of other physicians with far from satisfactory results, and subsequently long trials of therapy with various methods under the author's care, with the usual tendency to seasonal recurrences and varying degrees of difficulty in controlling the symptoms. Several of the patients had had recurrent bouts of hemorrhage of various degrees. Robuden injections and pills were given to several of the patients during the bleeding with rapid subsidence of this manifestation during the course of the treatment. Whether this represents a 'post hoc' or a 'propter hoc' manifestation only further observation can determine, but it appears to be fairly certain that the exhibition of Robuden is not contraindicated during bleeding. Thus the major portion of the patients concerned in this study were those who did not respond well to the various methods of therapy in standard use. The specific methods employed in the individual cases are stated in the case histories given.

The criteria employed in determining the efficacy of the treatment were: the length of time required for the control of symptoms; the degree of objective improvement as indicated by the X-Ray findings; the incidence of recurrence with the previous methods of therapy as compared with Robuden therapy. With the exception of Case 24 all patients were ambulatory and continued with their work.

The X-Ray evidence of healing of peptic ulcer is most readily demonstrable in gastric ulcer; in two of

the gastric ulcer patients there was very rapid healing of the ulcer with disappearance of the ulcer crater in less than two weeks in Case 23, and in Case 18 the abolition of symptoms in 12 days with complete freedom from symptoms to date of writing and absence of any radiologic evidence of the ulcer 5½ months after cessation of the treatment.

The patients included in this study consist of 24 duodenal ulcer patients; 7 gastric ulcers; three patients with ulcerative colitis and one with gastritis. Their ages range from 25 to 65. Very limited dietary restrictions were imposed: the avoidance of fried, pickled and smoked foods; the use of alcohol was not prohibited provided it was taken in moderation and either with, or preceded by, a glass of milk. Adjuvant forms of therapy, such as small doses of phenobarbital and antacids were employed where indicated, after a week or so of Robuden therapy. Each patient received from 15 to 20 intragluteal injections of Robuden, usually 1 cc. three times weekly. In the absence of definite subjective improvement after five injections, the dose was increased to 2cc. or the injections were given daily. The insoluble fraction of the Robuden preparation was taken in the form of pills, one being taken three times daily, and continued for three to four weeks after cessation of intramuscular therapy. At this stage of the therapeutic course the patients were instructed to continue with the dietary regimen and to avoid excesses; to return the following spring or fall, as dictated by circumstances, for a short additional course—six to eight intramuscular doses and three tablets daily for three to four weeks. About a third of the patients returned for further treatment, the rest were communicated with, some returning for a prophylactic course, others preferring to wait for evidence of recurrence. The incidence of such recurrences is indicated in Chart No. 1.

RESULTS

Of the 20 duodenal ulcer patients treated for periods ranging from 12 to 22 months (two for a shorter period) with Robuden as indicated above, 15 were completely controlled (complete alleviation of symptoms with none or very mild, easily controllable, seasonal recurrences). Three of the cases were partially controlled (more definite and/or more frequent recurrences). There were two failures; in Case 2 surgical intervention was necessitated by the presence of pyloric obstruction; Case 10 did well for a time and relapsed under severe economic difficulties; a second course of Robuden failed to give relief. Of the six gastric ulcer patients, the ulcer of Case 23 healed completely, symptomatically and radiologically, within 10 days (Figs. 1 and 2); that of Case 18 showed complete healing radiologically and the patient has remained asymptomatic to date; Case 24 obtained excellent results in the control of symptoms but not in maintaining the improved status for any great length of time without recourse to additional Robuden therapy. Tables 1 and 2 indicate the course and results of the treatment employed.

Three of the patients who returned without being recalled, 4, 14 and 21, requested additional Robuden therapy because during the time elapsed since completion of the course, they had enjoyed more complete

Fig. 1, Case 3: X-Ray findings Apr. 17/52, prior to Robuden therapy. Note marked deformity and large crater of duodenum.

Fig. 2, Case 3: X-Ray findings July 10/52, after Robuden therapy. Note absence of deformity and crater.

TABLE I

Case	Sex	Age	Site and Duration	Previous Therapy	Recurrences	Response to Robuden			Recurrence	Time Under Treatment
						Good	Fair	Poor		
1. A. T.	M	47	D(1) 15 years	Sippy, Banthine	1-2 annually	Good(5)			None	22 months
2. W. A.	M	65	D(2) 17 years	Sippy, Banthine	1-2 annually			Poor(5)(3)	Three	18 months
3. S. N.	M	36	D(1) 15 years	Sippy, nembut., morph.(4)	Frequent	Good(5)			One (mild)	22 months
4. L. B.	M	61	D(2) 30 years	Sippy, Banthine, etc.	Frequent	Good(5)			None	22 months
5. A. C.	M	59	D 20 years	Sippy, Sedatives	Frequent	Good(5)			None	20 months
6. J. G.	F	34	G 6 years	Sippy, Sedatives	Frequent		Fair		One	15 months
7. M. G.	M	50	D 2 years	Sippy, Sedatives	Two	Good(5)			None	22 months
8. I. K.	M	39	D 8 years	Sippy, Robuden(6)	Frequent		Fair		None(7)	22 months
9. R. L.	F	40	D 9 years	Sippy, Banthine, Sedat.	Frequent		Fair		Two (mild)	21 months
10. T. K.	M	33	D 3 years	Sippy, Banthine, Sedat.	Frequent	Good			One	15 months
11. S. C.	M	43	D 5 years	Sippy, Sedatives	Frequent two years	Good			None	16 months
12. J. F.	M	37	D 2 years	Sippy, Sedatives	Two	Good(5)			One (mild)	15 months
13. E. H.	M	51	D 10 years	Sippy, Sedatives	Frequent	Good			One (mild)	19 months
14. E. M.	M	54	D 15 years	Sippy, Sedatives, Banth.	Frequent	Good(5)			One (mild)	16 months
15. C. S.	M	52	D 8 years	Sippy, Sedatives	Frequent	Good			Mild	15 months
16. L. S.	M	49	G 5 years	Sippy, Sedatives, Banth.	Very Frequent			Poor	Several	12 months
17. C. P.	M	44	D(1) 9 years	Sippy, Sedatives	Frequent	Good			One (mild)	16 months
18. T. H.	M	43	G 9 years	Sippy, Sedatives	Frequent	Good			None	7 months
19. D. R.	F	36	D 6 years	Sippy, Sedatives, bellad.	Frequent		Fair		One (mild)	22 months
20. E. B.	F	45	G 10 years	Sippy, Sedatives	Frequent	Good			None	14 months
21. M. I.	M	45	D 8 years	Sippy, Sedatives, Probanth.	Frequent	Good			Several (mild)	18 months
22. D. G.	F	36	D 6 years	Sippy, Sedatives	No relief	Good			Mild	19 months
23. E. W.	M	49	G 8 mos.	None	.....	Good			None	15 months
24. J. B.	M	60	G 19 years	Sippy, Sed., Banth.	Frequent		Fair		Mild	17 months
25. E. C.	M	46	D 6 years	Sippy, Sedatives	Seasonal	Good			None	7 months
26. J. L.	M	25	D 2 years	Sippy, Amphogel, etc.	No relief			Poor	No relief	9 months
DISEASES OTHER THAN PEPTIC ULCER										
27. J. P.	M	42	Gastritis 4 years	None			Fair		.....	9 months
28. J. P.	M	26	U. Colitis 4 years	Ileostomy	Rect. bleed.	Good			None	7 months
29. N. O.	M	23	U. Colitis 5 years	Diet, Vitamins	Const. 1 yr.		Fair		Yes	13 months
30. X.	F	20	U. Colitis 2 years	Diet, Vit., Chlomyc., Acth, Terramyc.	Const. 7 mos.		Fair		Incomp. relief	15 months

(1) Hematemesis or melena on one or more occasions. (2) 30% or over 6 hr. retention. (3) Surgical intervention. (4) Prior to treatment had been receiving Nembutal suppos. & hypos. of Morphine. (5) Seasonal prophylactic Robuden therapy. (6) Patient had had Robuden therapy in Europe four years previously. (7) Only slight relief while on treatment, but improvement progressive and patient has remained well to present time.

freedom from ulcer symptoms for a longer time than with any previous form of therapy.

A number of the patients commented on the increased appetite during the course of the treatment; in some of the patients the weight gain was considerable, eight of the patients showing gains between 5 and 44 lbs. There was no significant gain in the rest of the group.

An interesting phenomenon occurred in three of the patients. Patient No. 18 had an unstable colon syndrome with a tendency to diarrhea, in addition to a gastric ulcer. Under Robuden therapy the ulcer pains were eliminated, but the left-sided lower abdominal pain persisted, i.e. in this instance, abdominal pain other than that due to the peptic ulcer was not relieved by Robuden. Case 5 with spastic colon in addition to a duodenal ulcer, obtained complete and persistent relief from the ulcer pains under the Robuden treatment, but the pain associated with the spastic colon remained unaltered; conditions were similar in Case 21. Such therapeutic dissociation of two coexisting pains of different etiology, one produced by peptic ulcer, the other by a functional disturbance, appear to the author to be not without significance as indicating a specific, selective therapeutic effect. In all three instances the functional disturbance could be relieved by the exhibition of phenobarbital with belladonna, the opportunity to do so arising on more than one occasion in each of these patients.

The single patient with gastritis was difficult to evaluate convincingly except on a purely subjective basis—he stated that he benefited considerably from the treatments; it is hoped to evaluate the effect of Robuden on a group of gastritis patients. The same thing may be said in reference to the effect on ulcerative colitis patients; there is very little that one can say with justification, since only three such patients were observed. It is, however, desired to record in this preliminary report that Robuden appears to have the faculty of diminishing or arresting bleeding in ulcerative colitis just as it apparently does in melena of peptic ulcer origin.

ILLUSTRATIVE CASE HISTORIES

Case 1. Mr. A. T., tailor. Seen in 1938 at age of 32, for severe hematemesis and melena, giving a history of symptoms, mild in degree, suggestive of duodenal ulcer. Diagnosis confirmed after arrest of hemorrhage. The ulcer symptoms were readily controlled on a modified Sippy diet and antacids and he remained relatively asymptomatic until Sept. 1945 when he had a moderately severe recurrence of the bleeding. Between 1945 and Mar. '51 he had had three additional, moderate hemorrhages. In April '51 Banthine therapy was instituted; responded moderately well but had another hemorrhage on the 4th of Feb. '52. After arrest of the hemorrhage he was placed on Robuden therapy. Within a week he was free from symptoms, and following termination of Robuden therapy he was instructed to take Neutrasil powder three or four times daily. He was given a prophylactic series in Sept. '52, Feb. and Sept. '53 and has been free from all but very minor symptoms; has had no frank bleeding; stool examinations have been negative for occult blood; and the patient states that he had been generally better than in the two or three years preceding Robuden therapy.

Case 2. Mr. W. A., age 51, June '39. Lumber merchant. Typical ulcer syndrome of several years duration. Duodenal ulcer with 40% six hour retention was demonstrated radiologically. He responded moderately well to a modified Sippy diet and antacid therapy and remained well except for mild seasonal recurrences until the spring of 1945. From 1945 to 1951 the recurrences became progressively more severe, and were not as readily controlled. A small deformed cap was visualized radiologically, this time without six hour retention. The symptoms were controlled with some difficulty on a strict diet, atropine and phenobarbital, Neutrasil and Amphojel. Following this he was only moderately well and returned a year later with severe day and night pain and vomiting. Robuden therapy was instituted Apr. 8, '52, the patient receiving no other therapy. The pain, nausea and vomiting disappeared completely within a week. By the seventh injection he stated he "felt 100%." The course consisted of 18 injections and one pill three times daily for a month. In mid July, following a 300 mile trip over very rough roads, he felt ill, complaining of severe burning in the upper abdomen and lower chest and vomited brown material. The stool was negative for occult blood and the R.B.C. and Hgb. were within normal limits. He was given an additional series of 6 Robuden injections and 3 pills daily for three weeks; complete relief was achieved by the second week. He remained well and was not seen until Feb. 20, '53 stating that he was tired, had many worries and a succession of colds. Toward the end of July he developed a severe recurrence associated with a great deal of vomiting, anorexia and pronounced fatigue. In view of the severity of the symptoms and lack of consistent response to any form of therapy tried, surgical intervention was advocated. He has remained perfectly well since.

Case 3. Mr. S. Contractor. First seen at the end of 1951; age 34. For many years he had been subject to "stomach trouble," relieved by bicarbonate of soda. The symptoms had a tendency to occur in the fall, to last several weeks and to become more severe in the preceding two years. When first seen the patient had been confined to bed for six weeks because of the severity and intractability of the symptoms initiated by melena four months previously. Appropriate diet, antacids and sedatives having failed, the physician in charge resorted to nembutal and frequent hypodermic injections of morphine. X-Ray examination revealed a moderately large duodenal ulcer (Fig. 1). Getting the patient out of bed and weaning him of narcotics, while difficult, was much less so than anticipated. Reassurance, convalescent Sippy diet, ¼ gr. phenobarbital three times daily and an antacid powder alternated with an alkaline powder gave considerable, but not complete relief. During the following 10 days he had been given a total of 17 capsules containing ext. Belladonnae gr. 1/6, amidopyrine grs. 2½, occasionally with codeine phos. gr. ¼, resulting in additional improvement. He returned from an exhausting business trip in Mar. '52 complaining of frequent bowel movements; these were black and 4 plus benzidine positive. R.B.C. 3.5 mil., Hgb. 54%. Following bed rest and

control of the bleeding Robuden treatment was started on the 18th of Apr. Improvement was rapid after the 4th injection and within one month he had gained 20 lbs. in weight. On June 3rd tarry stools recurred. The bleeding was readily controlled, following which he received six additional injections of Robuden. By mid-July his weight had increased from 163 to 185 lbs. In Sept. '52 he received a prophylactic course of six injections and three tablets daily for two weeks. He was then returned to the referring psychiatrist who informs me that he has remained well to date of writing. Fig. 2 demonstrates the appearance of the duodenum on the 10th of July '52, there was no evidence of ulcer at this time.

Case 4. Mr. L. B., merchant; present age 61; first seen in 1926 at age 34. At the time he had rather indefinite gastric complaints which had been diagnosed as duodenal ulcer, but this diagnosis could not be confirmed. He did well on low residue diet, sedatives and atropine in moderate doses. He was seen periodically with similar complaints and negative X-Ray findings. In Nov. '46 he developed for the first time postprandial epigastric pain, relieved by food. A duodenal ulcer with six-hour retention was demonstrated at this time. He did not respond well to standard forms of therapy—the relief was inconstant and transitory. Banthine was given a prolonged trial in 1951, the patient taking eight tablets daily with some relief for a time, but later having to support the effect of Banthine by taking Donnatal as well. He returned in Apr. '52; he was now troubled with occasional night pain and penetration of the pain to the back. An irritable cap and a moderately large crater were demonstrated on X-Ray examination, but there was no six hour retention at this time. On the 22 Apr., 1952 he was placed on Robuden therapy without consistent improvement during and after a course of 15 injections and the usual dose of Robuden pills. He was not seen again until Jan. 9, '53 when he reported that he had been well, better than in a long while, and requested another course of Robuden although he was asymptomatic at the time. When reminded that the first course did not appear at the time to do very much for him, his answer was that after the course of injections he began to show progressive improvement and at the beginning of January realized that for the first time in several years he had been free from pain for seven months, including the fall of 1952. He was given a short course. Sept. 24, '53 he reported slight discomfort in the epigastrium but never pain, during the preceding two weeks. He had been taking antacids during this time and desired another course of Robuden, which he received between Sept. 24th and Oct. 26th. He has had no complaints to date.

Case 7. Mr. M. G.; age 50 Mar. '52. The patient presented an atypical symptom complex of almost two years duration, suggesting several possibilities, including coronary disease and mid-dorsal arthritis. A moderately large duodenal crater was demonstrated radiologically. He received 1cc. Robuden three times weekly for 20 doses and three tablets daily for 2½ mos. Pronounced improvement was noted by the time he had received the fifth injection. Two weeks after cessation of the intramuscular therapy, he suffered a slight recurrence following a gross dietary indiscretion; this was quickly corrected by reverting to his diet. He returned for prophylactic courses in Sept., '52, in Feb., '53 and in Oct., '53. He had remained asymptomatic until just prior to returning in October; became symptom-free after the second dose of Robuden and has remained so to the time of writing.

Case 9. Mrs. R. L.; housewife, age 40 in 1951. Had been treated for duodenal ulcer for a period of several years. The symptoms were typical and moderately severe. She had been on Amphojel, antacids and a combination of phenobarbital and belladonna with inadequate and inconstant relief. At the time the patient was first seen she was anemic with a red cell count of 3 mil. R.B.C. and a Hgb. of 50%; gave a history of recent tarry stools but stools at time of investigation were negative for occult blood on several successive examinations. A large duodenal ulcer was revealed radiologically. There was some improvement on Banthine, 50 mg. four times daily, but moderately severe pain persisted and Neutrasil was added. She continued on this treatment through Apr. and May with only partial relief, and was troubled with persistent headaches which disappeared when she stopped taking Banthine. At this time she was placed on Robuden therapy; she showed definite improvement after the second injection and remained well following a full course until Feb. '53 at which time a mild recurrence had occurred. She was given a short course of Robuden with a similar rapid relief. In the fall of 1953 she had another mild recurrence. She requested another course of Robuden stating that since institution of this treatment "the ulcer is much easier to live with." At the time of this report she is well.

Case 14. Mr. E. M., merchant; first seen June 1940 at the age of 39. Had been treated for ulcer since 1938 and had been relatively well on treatment until spring of 1939. He presented a typical duodenal ulcer history; the X-Ray examination revealed an uncomplicated duodenal ulcer. Except for minor discomforts he improved materially on a modified Sippy diet, sedatives and antacids. He was seen periodically for mild recurrences and one or two moderately severe ones until the spring of 1949 when the symptoms returned in a fairly severe form. These were controlled with more difficulty than on previous occasions and the same difficulty was encountered with a similar recurrence in the fall of the same year. He was not seen again until Jan. '52 stating that he had had considerable difficulty in controlling the ulcer symptoms and that he had tried Banthine with relief in the spring of 1951. Moderately severe symptoms returned in the fall of 1952. Banthine failed to give relief this time and the patient was again placed on a rigid diet, magnesium trisilicate, and belladonna with phenobarbital. Relief was only partial and Robuden therapy was instituted. At the same time he was placed on a more generous diet (only fried, pickled, smoked and highly spiced foods and meat extractives being excluded). He responded quickly to Robuden therapy and after 10 injections and pills for six weeks he remained asymptomatic until Dec. '53 when he requested another course of Robuden for a mild recurrence because he had had a very comfortable year after the first course. On the 19th of Jan. he was free from discomfort after the 4th injection.

Case 20, Mr. T. H., accountant, age 37 in 1947. When first seen in June '47 the history was not characteristic of peptic ulcer, but presented suggestive symptoms: periodic cramps and diarrhea lasting a day or two and recurring every two or three months; persistently recurring sense of discomfort in the epigastrium, suggestive of hunger. He was found to be hyposensitive to pain. A well-defined prepyloric ulcer with 50% six hour retention was revealed on X-Ray examination. He was given general advice, placed on a strict diet, sedatives, antacids and atropine. He followed this treatment for six months and remained well during this time when he began to be lax in following the treatment and developed a severe recurrence associated with the vomiting of sour gastric contents. In spite of reverting to more careful observance of his instructions, recurrences occurred in the spring and fall of every year. Robuden therapy was instituted in June 1953 at which time he weighed 116 lbs. Because of the severity of the symptoms he was given a daily injection of lcc. for 15 doses and one pill of Robuden three times daily until the end of Aug. At this time he was instructed to take one or two Gelusil tablets three times daily. He returned in mid-December 1953 stating that he had remained well. During this time his weight had increased to 160 lbs., a gain of 44 lbs. There was no radiologic evidence at this time of the ulcer demonstrated six months previously. (Figs. 3 and 4).

Case 22, Mr. J. B., unemployed, age 46, Aug. 1937. He was troubled for years with pain in the epigastrium, two or three hours after meals. Peptic ulcer could not be demonstrated radiologically in 1945. In Aug. '41 he had a splenectomy for splenic cyst. He continued to complain of R.U.Q. and epigastric pain. The gall bladder, stomach and duodenum were negative on several additional X-Ray examinations, but in Apr. '48 a gastric ulcer on the lesser curvature of the pars media was demonstrated. The symptoms gradually increased in intensity in spite of antacids and sedatives; by July 1950, however, he was better. In the fall of that year the severe pain returned and again from Apr. into Aug. '51. During this time and into Jan. '52 he had been on Banthine and codeine phosphate without noteworthy improvement. In July chloral hydrate in 5 gr. doses t.i.d. brought some relief. In Sept. the pain became very severe again and he was hospitalized. The ulcer was again demonstrated and he was started on a course of Robuden therapy. There was considerable improvement after the third dose and the patient was discharged to be followed in the O.P.D. Improvement continued with occasional slight day or night pain. By Oct. 1952 he had received 18 injections, and at this time had an upper respiratory infection, with the temperature rising to 102, but was free from ulcer symptoms. On the 25th of Sept. the ulcer could not be demonstrated radiologically. The patient at this time stated that the treatment had given him an appetite, something he had not had for 10 years. Robuden therapy was discontinued in Dec. '52 and the patient returned a short time later complaining of a recurrence of the pain and of vomiting. Resumption of Robuden therapy was instituted at his request. Within two weeks he was free from symptoms and continued so until the beginning of April when he was again given Robuden until the middle of June. The pain returned in Aug. but there was no X-Ray evidence of recurrence. He was placed on three tablets

Fig. 3, Case 20: X-Ray findings prior to Robuden therapy —prepyloric ulcer.

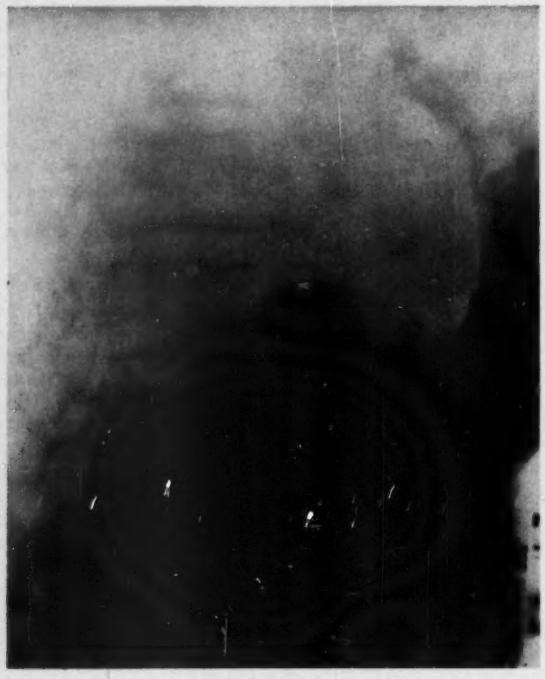

Fig. 4, Case 20: X-Ray findings after Robuden therapy. Healing of the prepyloric ulcer has occurred.

of Antrenyl (Ciba) with some relief, but preferred Robuden for the greater relief. This was done, the patient receiving the last dose Oct. 5, '53; he was still free from pain in January.

Case 23. Mr. E. W., age 49 in Oct. '52. Griping pain of one month's duration; relation to food indefinite. Loss of 5 lbs. in weight. Anorexia. An ulcer on the posterior wall of the media portion close to the lesser curvature was found on X-Ray examination (Fig. 5). The patient was placed on Sippy diet and on Robuden. Subjective improvement was quite marked after five injections, and X-Ray examination at that time failed to visualize the previously seen ulcer (Fig. 6). After the 18th injection he was again examined radiologically on Dec. 15th and also Feb. 4, '53, on both occasions with negative findings. He has remained well since.

DISCUSSION

While one cannot draw absolute conclusions from so small a series, the patients selected for this study were chosen very carefully with a view of obtaining fairly definite answers to clearly stated questions:

1. What can this form of treatment do for ulcer patients who have had various forms of therapy over a period of years (ranging from 2 to 30 in this series), with less than satisfactory results?

2. Can this form of treatment do anything more for the patient than can be accomplished by the prevailing forms of medical therapy?

3. Can it protect patients from choosing the surgical solution as a measure of desperation, when clinical judgment, in the absence of acceptable surgical indications, favours the non-surgical approach?

These questions can be answered affirmatively with but few qualifications:

1. When it is considered that most of the cases chosen for this trial were patients who had had ulcer for a long time and had not been satisfied with the results obtained up to that time, the achievements obtained are revealing: of 20 patients with duodenal ulcer 15 did very well; 3 were better than they had been on previous forms of therapy, and only two failed to improve. Two of the patients in this group came to operation, Case 2 with legitimate indications, Case 26 because he was tired of medical treatment. This patient had a severe hemorrhage on the 5th day P.O., and three months after operation feels "not too strong," and on several occasions had symptoms suggestive of dumping syndrome. Of the gastric ulcer

Fig. 5, Case 23: X-Ray findings prior to Robuden therapy. Large ulcer crater in the pars media of the stomach.

Fig. 6, Case 23: X-Ray findings after Robuden therapy. Note complete healing of ulcer.

patients 3 did well, in 2 the results were fair and poor in 1. (Table 2.)

TABLE II

	Number	Good Results	Fair	Poor
Duodenal Ulcer	20	15 (75%)	3	2
Gastric Ulcer	6	3 (50%)	2	1
Ulcer, Colitis	3	1 (33%)	2	0
Gastritis	1	0	1	0
Total	30	19 (63%)	8	3

A rather interesting feature associated with this study is the fact that about 25% of the patients in this group returned for seasonal prophylactic treatment, even in the absence of recurrences, while the same patients had not done so in the past when instructed to return.

2. One of the difficulties associated with the medical treatment of peptic ulcer is the dietary monotony. It has been found that more leeway can be given in the matter of diet when the patient is on Robuden therapy. A fair proportion of patients showed considerable increase in weight. One of the advantages of this form of treatment stressed by the Swiss reports is its effectiveness in ambulatory patients; our experience has been similar. The selective action of Robuden in the elimination of pain of ulcer origin but not of intestinal pain of non-ulcer origin, as demonstrated in three of the patients, constitutes interesting evidence in support of the specificity of Robuden action.

3. The third question is automatically answered in the improved results obtained with this form of therapy.

If the highly encouraging results obtained in this group of patients should be confirmed in studies on a larger series observed for a longer period of time, this therapeutic approach gives promise of an extremely valuable addition to available methods of treating the peptic ulcer disease.

SUMMARY AND CONCLUSIONS

1. The history of the use of gastroduodenal extracts in the treatment of peptic ulcer has been briefly reviewed and the relation of Robuden to other extracts considered.

2. The method of evaluating the effect of Robuden on the specific material selected for this study is described.

3. The utilization of each long-observed patient as his own control was adopted.

4. With a single exception, the treatment was ambulatory.

5. The therapeutic efficacy was judged by the length of time required to control the symptoms; the degree of improvement revealed by X-Ray examination; and the incidence of recurrence as compared with that observed prior to the use of Robuden.

6. The material consisted of 20 duodenal and six gastric ulcer patients, varying in age from 23 to 65; three patients with ulcerative colitis; one with gastritis.

7. Fifteen to twenty 1 or 2 cc. intramuscular injections 3 to 7 times weekly for a total of 15 or 20 injections, and one pill 3 times daily for 4 to 6 weeks constitute the usual initial course.

8. A prophylactic course of 5 to 10 injections and three pills daily for about a month has been found to be highly beneficial in avoiding seasonal recurrences or in arresting them quickly should they occur.

9. With the exception of two, all patients have been under this treatment for periods ranging from 12 to 22 months.

10. Of the 20 duodenal ulcer patients, 15 were completely controlled; 3 were partially controlled; there were 2 failures.

11. Of the 6 gastric ulcer patients, 3 had good results; 2 were improved; in one case the results were poor.

12. There was a tendency to improved appetite and gain in weight in a significant proportion of the patients.

13. Three of the patients exhibited an interesting phenomenon, namely, evidence of a selective therapeutic effect of Robuden, leading to therapeutic dissociation of two coexisting pains of different origin, one caused by the ulcer disease and relieved by Robuden the other caused by functional disturbances of lower intestinal segments and unaffected by Robuden.

14. Nine representative case histories are given.

15. Among the reported advantages of Robuden therapy are the highly satisfactory results obtained with ambulatory treatment; a second, not to be minimized advantage is that the dietary regimen can be more generous than with other forms of therapy.

16. The results obtained in this small series of patients warrants further studies on a larger series for a longer period of time.

The assistance of Robapharm Laboratories, Basel, Switzerland, in carrying out this investigation is gratefully acknowledged.

Dr. Philip Levitsky followed and recorded the findings in two of the cases reported.

REFERENCES

1. Rivers, A. B.: Am. J. Digest. Dis., 2:189, 1925.

2. Stalker, L. K., Bellman, J. L. and Mann, F. C.: Ibid., 3:822, 1937.

3. Morrison, L. M.: Ibid., 8:361, 1937.

4. Ivy, A. C. and Gray, J. B.: Cold Spring Harbor Symposia on Quantitative Biology, 5:405, 1937.

5. Gray, J. S., Bradley, W. B. and Ivy, A. C.: Am. J. Physiol., 118:463, 1937.

6. Sandweiss, D. J., Saltzstein, H. C. and Farbman, A. A.: Am. J. Digest. Dis., 5:24, 1938.

7. Idem, Am. J. Digest. Dis., 6:6, 1939.

8. Sandweiss, D. J. Sugarman, M. H. Friedman, M. H. F., Saltzstein, H. C. and Farbman, A. A.: ibid., 8:371, 1941.

9. Culmer, C. V., Atkinson, A. J. and Ivy, A. C.: Endocrinol., 24:631, 1939.

10. Necheles, H., Hanke, M. and Fantl, E.: Proc. Soc. Exper. Biol. Med., 42:618, 1939.

11. Friedman, M. H. F., Saltzstein, H. C. and Farbman, A. A.: Proc. Soc. Exper. Biol. Med., 43:181, 1940.

12. Friedman, M. H. F., Reeknogel, R. O., Sandweiss, D. J. and Parkson, T. J.: ibid, 41:509, 1941.

13. Grossman, M. I.: Physiol. Rev., 30:33, 1950.

14. Friedman, M. H. F.: Amer. J. Digest. Dis., 17:99, 1950.

15. Sandweiss, D. J.: Gastroenterol., 1:965, 1943.

16. Friedman, M. H. F.: In Postgraduate Gastroenterology, edited by H. Bockus, Phila., 1950, Saunders & Co.

17. Idem., Vitamins and Hormones. Vol. IX, p. 113, 1951.

18. Ivy, A. C.: Am. J. Digest. Dis., 8:361, 1941.

19. Idem.: Feder. Proc., 4:222, 1945.

20. Greengard, H., Atkinson, A. J., Grossman, M. I. and Ivy, A. C.: Gastroenterol., 7:625, 1946.

21. Sandweiss, D. J.: J.A.M.A., 138:552, 1948.

22. Pollard, H. M.: Arch. Surg., 56:372, 1948.

23. Wollum, A. and Pollard, H. M.: Gastroenterol., 17:535, 1951.

24. Kirsner, J. B., Levin, R. E. and Palmer, W. L.: ibid., 10:256, 1948.

25. Wirts, C. W. and Friedman, M. H. F.: Federation Proceed., 8:169, 1949.

26. Ferayorni, R. R., Code, C. F. and Morlock, C. G.: Gastroenterol., 11:730, 1948.

27. Bone, F. C., Cassel, C., Ruffin, J. and Reeves, R. J.: Ibid., 17:35, 1951.

28. Friedman, M. H. F., Saltzstein, H. C. and Farbman, A.A.: Proc. Soc. Exper. Biol. Med., 43:181, 1940.

29. Friedman, M. H. F. and Sandweiss, D. J.: Am. J. Digest. Dis., 8:366, 1941.

30. Haskell, B. F. and Friedman, M. H. F.: Am. J. Surg., 76:709, 1948.

31. Friedman, M. H. F.: Federal Security Agency, United States Public Health Service Progress Report, 1952.

32. Gill, A. M.: Lancet, 2:202, 1945.

33. Friedman, M. H. F., Haskell, B. F. and Waldren, J. M.: Fed. Proc., 7:37, 1948.

34. Schmassmann, H.: Schweiz. med. Wschr., 74:576, 1944.

35. Ivy, A. C.: Am. J. Digest. Dis. & Nutr., 8:361, 1941.

36. Gray, J. S.: Ibid., 8:365, 1941.

37. Burghartz, N.: Klin. Wschr., 31:543, 1949.

38. Roulet, F.: Schweiz. med. Wschr., 41:912, 1945.

39. Idem: Schweiz. med. Wschr., 33:748, 1949.

40. Vallery-Radot, P., Halpern, B. N. and Martin, J.: Presse med., 17:185, 1947.

41. Neumayr, H. and Schmid, J.: Gastroenterologia, 74:121, 1949.

42. Riefler, F. and Schmid, J.: Ibid., 74:133, 1949.

43. Stolka, J. B.: Lancet, 259:858, 1950.

44. Herzog, A.: Schweiz. med. Wschr., 79:121, 1949.

45. Surkes, A. W.: Praxis, 21:1947, quoted by Schmassmann.

46. Schmassmann, H.: Schweiz. med. Wschr., 81:166, 1951.

47. Neumann, H.: Ibid., 29:653, 1946.

48. Burghatz, N.: Aertztliche Wschr., 22:6, 1951.

49. Friedman, M. H. F.: Personal communication.

THE NUTRITIONAL FACTOR IN DEPRESSIVE STATES

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IN THE past, psychosomatic problems have been approached from the point of view of either the psychological or the mechanistic theories of causality. The psychological approach tries to evaluate and solve the problem of neurotic and somatic changes on the basis of dynamic disturbances. The mechanistic approach, on the other hand, attempts to explain psychic and somatic changes on the basis of pathological changes in structure, chemistry and in physical disturbances of anatomical arrangements. More recently, however, the *total personality approach* attempts to look upon the patient as a *whole functioning and integrated unit,* in which defects in function are given greater importance than any single anomaly of psychological or organic nature.

NUTRITION

The position of the psychological schools of causality in psychosomatic disorders is strongly supported by the failure of the mechanistic school to produce substantial evidence from the pathological and clinical laboratory. In recent years, scientific knowledge of the definite role of nutrition in therapeutics has been growing. Nutrition has ascended from empiricism to scientific evaluation of nutrients and from cultism, such as vegetarianism, to practically applied dietary prescription writing, based on intensive studies of human nutritional requirements. Fundamental chemical, biophysical and biochemical evidence of sound scientific nature is now available and is providing the

needed evidence that had not been forthcoming from the mechanistic school.

The enzyme, cholinesterase, has recently been discovered on the surface of nerves. It is a normal constituent of the human body. When it is destroyed the nerves are paralyzed. Deficiency of cholinesterase gives rise to paresthesia and numbness, neuritis and probably paralysis of nerves. There is some doubt as to its being selective in its action on motor nerves alone.

When stress and strain, which often play an important role in lowering the patient's protective mechanism, *coexist with cellular or metabolic nutritional deficiency, a psychosomatic bridge transferring relatively somatic disorders into relatively psychic disorders, is constructed in all its elements:* (1) psychic predisposition and background, (2) lowering of protective mechanism tending to (3) changes in the capacity of nerve tissue to function "normally" due to a specific deficiency in essential nutrients. This results in a full blown state of neurosis or psychosomatic manifestation.

The pessimistic personality is primarily one in a state of anxiety, a form of fear that leads to dejection and depressions of various degrees. This type of personality, as a rule, requires unusual amounts of substitute or supplemental nutritional therapy to maintain a normal metabolic status. Evidence of this point of view is provided by Gorda and Wolff (1) in their study on the effect of vitamins in the synthesis of acetylcholine. It has been shown that this substance is of paramount importance in the transmission of nerve impulses. Too much or too little is responsible for changes in nerve conductivity with resulting exposure of neurotic symptoms.

Lowenbach and Greenhill (2) report the effect of feeding lactic acid and sodium lactate in milk to markedly depressed patients on the theory that these products of muscular exertion were identical with, and responsible for, the good effects of electroshock therapy. In 45 cases treated, 7 (15%) recovered, 5 (11%) showed marked improvement, 14 (31%) showed moderate improvement, and 19 (43%) remained unimproved. The immediate effect of lactic acid feeding was a short period of stomach distress which soon subsided and was followed by drowsiness and relaxation. Patients who previously required hypnotics were able to sleep without them. This is another example of nutritional therapy modifying psychic symptoms.

It still remains to be demonstrated that much of human behavior may be explained on endocrine and nutritional grounds and not necessarily on purely psychological grounds. Collip (3) demonstrated that removal of the pituitary gland in a wolfhound puppy caused the animal to lose his normal characteristics of aggressive behavior. Feeding of anterior pituitary extract caused the wolfhound puppy to become normal in behavior. Collip also relates the case of a diabetic patient, subject to hypoglycemic spells, who asked for help in a drug store because he was not in possession of sugar to relieve an oncoming hypoglycemic attack. His unsteadiness was misinterpreted as drunkenness and he was thrown out of the store. He became angry and was able to go to another for help, acting in a normal manner. The emotion of anger was responsible for the upsurge of sugar in his blood which overcame the hypoglycemic attack.

Rodis (4) considered that the symptom complex of depression followed a pattern of development as follows:

(1) Insomnia due to depressing thoughts
(2) Loss of appetite
(3) Changes in former interests and brooding
(4) Loss of sex urge
(5) Depression in spirit or mood—diurnal variation
(6) Ideas of suicide
(7) Fatigue and apathy
(8) Preoccupation with self
(9) Poor memory and inability to concentrate
(10) Indecisiveness
(11) Slowing of mental processes
(12) Feeling of impending evil, crying spells
(13) Facies of depression
(14) Previous state of good health
(15) Deception and covering up of symptoms

Niacin deficiency may give a similar picture and may produce "neurasthenia." Outstanding symptoms are:

(1) Weariness
(2) Apprehensive and pessimistic attitudes
(3) Sensitiveness to slight pressure over spine and pelvis
(4) Paresthesias, salty tastes
(5) Cramps
(6) Burning of eyes
(7) Insomnia and fatigue

Studies of the results of malnutrition in famine populations reveal the general occurrence of mental depressions and psychoses which are reversible when adequate nutrition is supplied in time.

The effects of nutritional substances have been studied in many other ways. Alcoholic intoxication has been shown to have a temporary stimulating and later a depressing effect on the central nervous system and circulation. Intoxication is satisfactorily being treated with glucose and high vitamin B complex. Alcohol is a high caloric substance and provides approximately seven calories per gram in metabolism. Its effect on respiratory quotient figures is more in the ketogenic field. Thus, fatty substances are not considered beneficial in depressions. This is true in diabetes where fats depress the diabetic metabolism and the insulin requirements. The depressing effect of fats is utilized in the ketogenic diets in the treatment of epilepsy.

Harris (5) reported a case of phenobarbital coma in which the patient responded slowly to glucose in-

TABLE

IMPROVEMENT OF SYMPTOMS BY TREATMENT WITH GLUTATHIONE-ENZYME SOLUTION

Case	Initials	Age	Sex	Medical Diagnosis	Psychiatric Diagnosis	Presenting Symptoms
1.	G. F.	53	F	Thyrotoxicosis Hypertension Glycosuria	Menopause Anxiety neurosis Phobias Hysteria	Insomnia Anorexia Fatigue Tension
2.	C. F.	61	M	Diabetes Post-U. R. I. Asthenia	Anxiety state	Anorexia Fatigue Sighing breathing Tension
3.	R. T.	56	F	Gall bladder disease CVR disease Obesity	Menopause Involutional Anhedonia	Insomnia Fatigue Sighing breathing Tension Cancerophobia Agitated Depressed
4.	R. S.	55	F	Diabetes Hyperthyroidism	Menopause Anhedonia	Insomnia Agitated Depressed Fatigue Sighing breathing Crying spells Tension
5.	C. F.	32	F	Rheumatic heart disease	Anxiety state	Fatigue Sighing breathing Premenstrual distress Tension Headaches
6.	R. N.	40	F	Mastectomy X-ray menopause	Neurosis	Fatigue Depressed
7.	L. S.	25	F	Chronic bronchitis Obesity Benzedrine poisoning	Anxiety neurosis Hysteria	Insomnia Depressed Sighing breathing Crying spells Premenstrual distress Emotional instability
8.	E. R.	61	F	CVR disease Gall bladder disease	Anxiety state	Insomnia
9.	B. P.	70	M	CVR disease Peptic ulcer	Anxiety state	Mild depression Insomnia Crying spells Cancerophobia Emotional instability Constipation
10.	M. E.	55	M	Hypertension	Anxiety state	Insomnia Phobias of h.b.p. Irritable Excitable
11.	A. B.	23	M	Xanthomatosis	Neurasthenia Gastric neurosis	Headaches Insomnia Depressed Crying spells Tension
12.	R. C.	47	F		Neurasthenia Phobias	Headaches Insomnia Depression Crying spells Menopausal distress Worried
13.	B. O.	60	F	Diabetes Cerebral hemorrhage Fibrosis of lungs	Anxiety state	Insomnia Nervous Marital problems
14.	D. A.	47	F	Hysterectomy Pulmonary Tbc. Diabetes	Psychoneurosis, Involutional Paranoid delusions Several stays in mental hospitals	Insomnia Crying spells Voluble talk

Case	Initials	Age	Sex	Medical Diagnosis	Psychiatric Diagnosis	Presenting Symptoms
15.	S. F.	40	F	Diabetes Chronic OMP	Anxiety state	Depressed Nervous Cries easily
16.	G. B.	58	M	Calcified G. B. Coronary H. D.	Anxiety state Phobias	Depressed
17.	E. K.	45	F	Diabetes Glaucoma	Paranoid type Anxiety state	Insomnia Depressed
18.	N. G.	54	F	Kidney disease in pregnancy Asthenia GB disease Hyperthyroidism	Psychoneurosis	Insomnia Anorexia Fatigue Weakness Cancerophobia
19.	C. G.	40	M	Neurocirculatory asthenia	Conversion hysteria Cardiac neurosis	Insomnia Fatigue Sighing breathing Tension Cardiac phobias
20.	F. G.	46	F	Diabetes CVR disease Hyperthyroidism	Conversion hysteria Neurosis	Insomnia Burning in throat Fatigue Dizzy spells Abdominal cramps
21.	N. S.		M	CVR disease Hypertension	Anxiety state Phobias	Insomnia Depressed Fatigue Tension
22.	A. K.	14	F	Benzedrine intoxication Hypothyroid Obesity	Anxiety state	Insomnia Depressed Sighing breathing Crying spells Premenstrual tension
23.	S. M.		M	Healed Tbc. Renal diabetes	Anxiety neurosis Anhedonia Phobias	Depressed Fatigue Sighing breathing
24.	E. E.	33	F	Obesity Benzedrine intoxication Thyroid adenoma		Insomnia Hunger Fatigue Irritable Compulsive food thoughts Dizziness Headaches
25.	C. M.	27	F	Obesity Benzedrine intoxication		Insomnia Premenstrual distress Headaches
26.	D. S.	43	F	CVR disease	Conversion hysteria Neurosis	Insomnia
27.	I. W.	58	F	Anemia	Psychoneurosis Anxiety state	Insomnia Anorexia Depressed Fears Tension
28.	E. S.	66	F	Diabetes Hypertension		Insomnia Anorexia Mild depression Fatigue Crying spells Menopausal distress Tension Cancerophobia
29.	E. K.	52	F	Hypertension Menopause GB disease Hyperthyroidism	Anxiety neurosis	Insomnia Depression Crying Spells
30.	J. G.	49	M	Bronchitis Chronic chlorine Poisoning	Post-traumatic neurosis Phobias Hysteria	Sighing breathing Tension

Case	Initials	Age	Sex	Medical Diagnosis	Psychiatric Diagnosis	Presenting Symptoms
31.	B. A.	66	F	Atrophic arthritis	Anxiety state Phobias	Insomnia Crying spells Tension
32.	B. A.	59	F	Amputation GB disease Hypertension Hyperthyroidism	Anxiety state Phobias Hysteria	Insomnia Anorexia Sighing breathing Crying spells Tension
33.	J. L.	42	M	Encephalitis Parkinsonism Hypertension	Anxiety state	Insomnia Anorexia Tremors
34.	G. L.	60	F	Ca of colon? Diabetes CVR disease	Anhedonia	Mild depression Insomnia Anorexia Fatigue Sighing breathing Cancerophobia
35.	A. D. C.	35	F	Fibrositis Fracture Rt. Hip	Post-traumatic neurosis	Insomnia Anorexia Depressed Fatigue Crying spells Tension
36.	S. S.	51	M	Renal diabetes CVR disease PVD disease Gastric neurosis Hyperthyroidism N. C. asthenia	Conversion hyst.	Loss of weight Depressed Fatigue Gastric conversion symptoms
37.	Y. B.	43	F	Diabetes Fibroids	Anxiety neurosis	Insomnia Tension
38.	H. C.	61	M	Induration of breast and nipple	Anxiety state	Insomnia Cancerophobia
39.	J. E.	72	F	Hypertension Coronary sclerosis	Anxiety state	Depressed Crying spells
40.	S. S.	55	M	Obesity N. C. asthenia (Patient has received electroshock treatment.)	Atypical paranoid involution Anhedonia	Anorexia Depressed Moody Crying spells Laughing spells Tension
41.	R. G.	29	F	Tubo-ovarian disease	Anxiety state	Insomnia Anorexia Crying spells Premenstrual distress Fear of insanity
42.	A. G.	50	F		Anxiety state Anhedonia	Insomnia Anorexia Depressed Crying spells Sighing breathing Fears
43.	L. S.	26	F	N. C. asthenia	Anhedonia Hysteria	Depressed Anorexia Crying spells Fears
44.	N. F.		F	Auricular fibrillation Arteriosclerosis	Recurrent senile psychosis	Insomnia
45.	M. M		F	Secondary anemia	Post-partum psychosis	Disturbed behavior

travenously and when Amigen (hydrolyzed protein containing amino acids) was administered intravenously, the patient went into collapse, which was successfully treated by readministering glucose and coramine (nicotinic acid derivative). Amino acids and proteins may be suspected in this case to be harmful in depressed cerebral conditions.

NUTRITIONAL THERAPY

The prevalence of evidence of metabolic and structural changes in depressions, schizophrenia and psychoneurosis appears to justify the impression that psychosomatic diseases have a reality basis in nutritional deficiencies as well as psychic and organic components. The *psychosomatic bridge* may be considered the soil in which psychic causes come to manifest themselves through the somatic structure or whereby somatic changes come to manifest themselves in psychic symptoms. Clinical evidence leads to the conclusion that the lack of certain essential nutrients seems to be responsible for the bridging, or somaticizing, or passing, of psychic into somatic symptoms. By creating certain changes in the nerve pathways, a lower threshold is established, thereby creating a pathway for the gradual or sudden emergence of psychosomatic syndromes. These specific nutrients would appear to be:

(1) Glucose

(2) Electrolytes, especially calcium and potassium

(3) Enzymes, carboxylases and hydrogenases

(4) Vitamins, factors in the vitamin B complex

Since glutathione, low in schizophrenics, is intimately concerned with oxygen transfer, it seemed logical to utilize it in cases of suspected or obvious psychosomatic disease since its action is quick and because it represents factors which, if deficient, are primarily concerned with the psychosomatic bridge. A parenteral preparation containing 50 mg. glutathione in 1 cc. of a solution consisting of metabolites from the respiratory enzyme cycle (still under experimentation) was developed and administered to a group of 45 cases which represents a substantial cross-section of patients with psychosomatic problems, or problems which have already been transmuted by crossing the *psychosomatic bridge;* i.e., neuroses, psychoses and borderline cases.

The effect of this administration was uniformly beneficial, particularly in reducing states of tension, anxiety, insomnia and nervous irritability. It acted as a safe, sedative medication in a manner similar to barbiturates but without the toxic side effects of the latter drug.

SUMMARY AND CONCLUSIONS

1. Ample clinical evidence has been gathered to indicate that deficiencies in specific nutrients may contribute to, or be responsible for, many psychic symptoms and may thereby become an important factor in psychosomatic disease, or even in organic pathological findings resulting from traumatic incidents.

2. Experience has shown that the needs of patients for a dietary regime must be satisfied before medical treatment can be considered complete. The tendency of a patient to lose his appetite is often the primary reason for calling on medical assistance. It is essential that a full medical as well as psychiatric history be obtained and a complete physical and psychiatric examination be made. In addition, exhaustive metabolic studies are necessary, and it is hoped that a metabolic investigation will be considered a routine necessity in every case of psychosomatic disease.

3. The use of a parenteral preparation containing 50 mg. glutathione in a solution of enzymes of the respiratory circle has given results not obtainable with other therapy in which a heightening of mood and a loss of depressive manifestations was observed. Improvement is defined here as a lessening of the anxiety and an occurrence of remission in varying degrees of the somatic complaints which did not respond to placebos.

REFERENCES

1. Gorda, C. and Wolff, H. G.: Effect of Vitamins on the Synthesis of Acetylcholine, Proc. Soc. Exper. Biol. & Med., p. 58, 163.

2. Lowenbach, H. and Greenhill, M. H.: Lactic Acid Feeding in the Treatment of Mental Disease, Victor News, 1946.

3. Collip, J. B.: Effect of Pituitary Glands on Man's Behavior, Science 9:84, 2176 (Sept. 11) 1936.

4. Rodis, I.: How is a Depression Diagnosed? Med. Ann. Dist. of Col., July 1945.

5. Harris et al: Case of Phenobarbital Coma, J.A.M.A. 131, 13:785, 1946.

STUDIES OF APPETITE AND OF CONSTIPATION IN ADVANCED LIFE: PSYCHOLOGICAL AND STATISTICAL EVALUATION OF A COUNTY HOME SURVEY IN IOWA

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THE GERONTOLOGICAL Unit of the Mental Health Institute of Cherokee, Iowa, in 1951 conducted a survey of county homes in four counties of Iowa with the purpose of obtaining data on psychiatric, psychological, and social factors related to the elderly residents of such institutions.

The nature of the survey made it possible also to obtain data regarding health factors and to study the information obtained in relation to other aspects of personality. This paper reports on appetite and bowel movement habits. The controversial nature of the information available in the geriatric literature regarding the factors of appetite and frequency of constipation in advanced life made it of interest to select these data of our survey for special study. For more detailed information about the general character of the survey as well as particular sections of it, the reader is referred to papers already presented, some of which have been published (1) (2) (3).

GENERAL INFORMATION

The survey covered county homes of O'Brien, Sioux, Webster, and Woodbury counties, all in the northwestern part of Iowa. The total number of residents of all age groups was 229, of whom the 126 (55 per cent) who were 65 years of age or over constitute our sampling. The mean age of the group surveyed was 75.21, the oldest being 96 and the youngest 65 years old. Eighty-seven were males and 39 were females. One hundred nineteen, or 94.4 per cent, had either never been married or were divorced or widowed. The majority had spent most of their lives in rural-farm areas; only 36, or 28.6 per cent, stated that they had lived predominantly in cities.

The investigators had to deal with a heterogeneous county home population, among them mentally ill and physically handicapped as well as physically and mentally normal individuals. The elderly persons included in the sampling were classified according to mental status as follows:

1. Normal (without psychosis), 47 (36.15 per cent).
2. Mildly mentally ill (with moderate mental symptoms or, although considered normal at time of interview, had mental hospital records), 23 (17.69 per cent).
3. Psychotic (with obvious symptoms of mental disease), 51 (39.23 per cent).
4. Unclassified (those who could not be placed in any of the first three categories), 5 (3.85 per cent).
5. Those who proved later to be under 65, 4 (3.08 per cent).

METHOD OF SURVEY

Data were obtained by means of a questionnaire utilized during and augmented by interviews. The questionnaire was based partly on the questionnaire "Your Attitudes and Activities," prepared by Burgess, Cavan, and Havighurst (3.a) and partly on one used in the medical survey conducted in Wolverhampton, England (3.b). Adjustments were made for local conditions and for the purposes of the Gerontological Unit, and some new questions were added.

In the case of the more normal residents, where good contact was possible, the questions and interviews were more detailed. In the case of psychotic residents the interviewers had to rely on less formal talks.

The normal and mildly mentally ill subjects were questioned separately and privately. At the beginning of the interview the subject was informed of the purpose of the survey.

Psychotic residents were usually interviewed by two members of the team, one of them a psychiatrist. In cases in which answers could not be obtained from the subjects, the steward or matron and in one case the registered nurse was called in and his or her information about the patient recorded.

No physical examinations were made. No other doctors were consulted about the physical condition of the residents.

I. APPETITE

Seventy-seven per cent of the normal and mildly mentally ill stated that their appetite was good, and almost 61 per cent of the psychotics were reported to have good appetite. (Table 1). In addition, most of those who reported only fair appetite usually enjoyed eating but objected to the kind of food they were receiving and/or had other reservations. In 12 cases, or 9.6 per cent, the answers had to be listed as questionable or undetermined. Of the latter group 11 were psychotics. Poor appetite was reported by 7.9 per cent, who included persons acutely ill and/or suffering from chronic gastro-intestinal conditions.

COMMENT

Two words are used to describe a person's desire

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TABLE I

APPETITE IN 126 ELDERLY COUNTY HOME RESIDENTS

Appetite	Mental Status									
	Normal	Mildly Mentally Ill	Total Normal and Mildly Mentally Ill		Psychotic	Unclassified	Total Psychotic and Unclassified		Grand Total	
			No.	Per cent			No.	Per cent	No.	Per cent
Good	36	18	54	77.1	30	4	34	60.7	88	69.7
Fair	7	4	11	15.7	5	....	5	8.9	16	12.8
Poor	4	1	5	7.2	5	....	5	8.9	10	7.9
Questionable or undetermined	....	....	....	....	11	1	12	21.5	12	9.6
Total	47	23	70	100.0	51	5	56	100.0	126	100.0

for food—hunger and appetite. It is, in fact, often difficult to distinguish between the two terms, yet they are basically different. Best and Taylor (4) define hunger as a "gastric sensation . . . due to the strong peristaltic contractions that arise in the stomach when it is empty or nearly so." Hunger can also be defined as a craving for food. However, a hungry individual may eat and satisfy his hunger without enjoying food or enjoying it very little.

Appetite is also based on a desire to eat and/or drink. In contrast to hunger, it is stimulated primarily by expectation of enjoyment. Appetite may or may not coincide with hunger. A person may have an appetite for ice cream or other sweets when he is not hungry and his stomach is full but craves the pleasure of eating sweets. As a rule, however, hunger and appetite appear together in a normally functioning organism.

Definition of appetite is complicated by a variety of factors not directly related to food intake and utilization. Many pathological conditions, such as cardiac decompensation, infectious diseases, blood dyscrasias, and other illnesses, depress appetite. Appetite may also be strongly affected by psychological reactions. Such conditions as anxiety, depression, preoccupation, restlessness, frustration, obsession, and many others, have an influence on the functioning of appetite. A person who has a good appetite today may lose it tomorrow, and restore it as soon as the causative depressant factors are removed. When a person is asked, however, whether he has good or poor appetite, the question has a specific and unmistakable meaning. Under good appetite is commonly understood a positive, and under poor appetite a negative, attitude toward food intake. A person who has a good appetite is usually hungry at regular intervals and enjoys eating. Indeed, he anticipates his future food intake and expects it to be enjoyable. A person with poor appetite is usually not hungry or, if he experiences the sensation of an "empty stomach," does not enjoy eating. The very thought of food intake may cause unpleasant feelings, even nausea.

Answers to questions regarding appetite are subjective, of course, but in view of the fact that the word "appetite" has a specific connotation it comes closer to being an objective criterion than any other subjective symptom in this area and may be used to some extent for orientation of the elderly person's general condition.

Appetite as such has rarely been explored in contemporary geriatrics. Much more interest has been devoted to studies of the secretions of the gastro-intestinal glands. Studies in the latter field indicate that in the majority of elderly individuals gastric secretion is diminished. It has been demonstrated that secretion of hydrochloric acid is particularly disturbed (5). Many investigators have therefore concluded that desire for food is lowered in elderly individuals (5). Stieglitz, who believes that appetite in advanced life is variable, writes that "in true senility it is often greatly depressed, roughly paralleling the gastric achlorhydria" (6). Some clinicians and investigators, as, for example, Boas (7), Thewlis (8), and others, who state that appetite in elderly persons is poor, ascribe it to, among other causes, the fact that the aged have a lessened sense of taste and smell.

Contrary to these opinions, data published by Griffin showed good appetite in 68 per cent and fair appetite in 14 per cent of the 129 elderly residents of a New England old age home (9). Sheldon, who conducted a house-to-house survey of elderly persons in the community of Wolverhampton, England, wrote that "In the great majority of instances the old people enjoyed their food. . . ." (10) In other words, the majority of his subjects had good appetite.

The present study indicates that the investigated elderly county home residents have no serious disturbances of either desire for or enjoyment of eating. Of the 126 persons investigated, 104 reported good or fair appetite, and poor appetite was found in only 10 persons, or roughly 8 percent of the sampling. All three members of the field work team were impressed by the almost unanimous and unequivocal reaction of the elderly residents to the question regarding appetite, whose statements were invariably confirmed by the county home personnel.

The data obtained were so self-evident that no statistical evaluation appeared necessary. It should

be noted that the general health of this group compared unfavorably with that of an average elderly community population. In this inquiry, for example, 20 persons out of a total of 126, or about 16 percent, were bedfast. (In the Sheldon community survey referred to above only 12 cases, or 2.5 per cent, were found to be confined to their beds). The implication is that the data obtained in the present survey are not only characteristic for a selected group but, contrary to the opinions of a number of experienced geriatricians, probably typical for the majority of the aged in general. The function of appetite appears to be well preserved in the elderly individual.

II. CONSTIPATION

Constipation is determined by two factors: frequency of defecation and consistency of the stool. Some authors feel that frequency of defecation is far less important in determining constipation than consistency of the stool. We agree with the definition given by Dock: "Constipation is evidenced by failure to move the bowels with the customary frequency, or by passage of rare, small, hard, and perhaps painful masses" (11).

Information on frequency of bowel movements was comparatively easily obtained. The investigated residents were asked to state the number of their bowel movements per day, and when evacuation was reported as less frequent than once a day, details were requested.

It was more difficult to achieve a degree of accuracy in determining consistency of the stool. A method had to be found that would permit statistical recording and evaluation of responses. A direct question regarding consistency, that is, whether the stool was hard, loose, watery, etc., was found to be impractical. Many do not pay attention to the character of their defecation; others have difficulty in determining what is hard, soft, etc.; and others are embarrassed or confused by this type of question and do not know how to answer. The Unit therefore substituted for a direct question an indirect inquiry using more colloquial, understandable, and psychologically acceptable terms. The residents were asked whether they were constipated, whether they were incontinent, and whether they had to use laxatives and/or enemas. In addition, the interviewers were instructed to record literally spontaneous remarks regarding bowel movements. A few examples may illustrate how the remarks were used for evaluation of types of evacuation. One resident stated that he had one bowel movement per day and considered himself non-constipated, but added that his stool was "not very loose." He was listed as non-constipated. Another considered himself non-constipated but admitted that he used enemas daily. He was classified as constipated. A third said that he had two to three bowel movements per day and considered himself somewhat constipated, but he had not been using laxatives. This response was classified as questionable.

The majority of answers, however, were definite and did not create any difficulty in tabulation.

The Unit felt that the method used to evaluate constipation, although based on subjective criteria, gave a reasonably accurate picture of the bowel movement habits of the elderly residents investigated.

RESULTS

The number of cases in which no data or questionable data were obtained was comparatively high—22 out of a total of 126. In these cases, which occurred mainly in the psychotic group, no decision could be made as to the character of bowel movements. The other 104 elderly residents were classified as either constipated or non-constipated, 22 being classified as constipated. (Table II.) Only 13 of these 22, however,

TABLE II

CONSTIPATION AND INCONTINENCE IN 126 ELDERLY COUNTY HOME RESIDENTS

Constipation and incontinence	Normal and mildly mentally ill		Psychotic and unclassified		Total	
	Number	Per cent	Number	Per cent	Number	Per cent
No. bowel movements per day						
Less than 1	12	17.1	2	3.6	14	11.1
1	32	45.8	16	28.6	48	38.1
2	14	20.0	7	12.5	21	16.7
3 or more	5	7.1	12	21.4	17	13.5
Questionable	7	10.0	19	33.9	26	20.6
Constipation						
Yes	17	24.3	5	8.9	22	17.4
No	48	68.6	34	60.7	82	65.2
Questionable	5	7.1	17	30.4	22	17.4
Laxatives	9	12.9	3	5.3	12	9.5
Enemas	1	1.4	....	....	1	0.8
Incontinence						
Yes	4	5.7	12	21.4	16	12.7
No	63	90.0	28	50.0	91	72.2
Questionable	3	4.3	16	28.6	19	15.1
Total number of subjects	70		56		126	

were taking laxatives or enemas, and only 14 had less than one bowel movement per day. In other words, a third of those who considered themselves or were reported by the personnel of the county home to be constipated and were so listed apparently had no particular difficulty with defecation. This would appear to demonstrate that the method used overestimated rather than underestimated the number who suffered from constipation. Even so, the number of constipated constituted only 17.4 per cent of the group. The non-psychotic and mildly mentally ill group showed the highest percentage of constipated (24.3) and the psychotic the lowest (8.9). It is probable that the number of persons listed as constipated is slightly high among the former and low among the latter. If the group of questionable responses is excluded the percentage of constipated becomes 21 and the non-constipated 79.

Approximately 13 per cent of the elderly individuals investigated were found to be incontinent. Here again

the psychotics prevailed. This figure is of comparative value. It was helpful in evaluating whether the respondent had spontaneous bowel movements. The survey team was doubtful, however, as to whether to consider the incontinence reported by the personnel as real incontinence. It is probable that shortage of personnel at the county homes was responsible for the "incontinence" of the psychotic patients. It was surprising, however, to find a number of incontinents among the non-psychotic and mildly mentally ill group (4 out of 70). This would appear to indicate that it is not always mental factors but often somatic factors that cause at least some of the incontinence found among elderly individuals.

STATISTICAL EVALUATION

The character of this inquiry made it possible to study constipation in relation to various manifestations of social and psychological behavior and other physical and mental conditions of the elderly county home residents. Statistical correlations of constipation with 15 other items were studied. Table 3 lists these items.

TABLE III

ITEMS WITH WHICH CONSTIPATION AND NON-CONSTIPATION WERE STATISTICALLY CORRELATED

A. Psychological factors

Whether or not the elderly resident:

1. Is resigned and hopeless
2. Wishes to leave the county home
3. Has plans for the future
4. Accuses himself or accuses other persons and circumstances
5. Feels old

B. Social behavior and activities

(a) Whether or not he communicates with the outside world
6. Is visited by former friends and relatives
7. Has severed relationships with former friends and relatives
8. Is taken care of by former friends and relatives

(b) Whether or not he participates in activities
9. Socializes with other county home residents
10. Works in or around the home
11. Is bedfast, is limited in movements, or moves freely

(c) Duration of institutionalization
12. Length of stay in the county home

C. Physical and mental health

Whether or not he

13. Suffers from physical invalidism or disease
14. Complains of insomnia
15. Has been an alcoholic

For statistical evaluation of items 1 to 11 and 13 to 15, the formula chi square was used to determine whether or not differences in the way the constipated and non-constipated groups aligned themselves under the various items were due to chance. It was found that, with one exception, the differences between the constipated and non-constipated groups in relation to all these items could be explained on the basis of chance. The exception was insomnia. It was found that the non-constipated group was significantly less affected by insomnia than the constipated. Table 4 shows that the probability of chance accounting for the differences was .05, so that, in statistical terms, we may reject the null hypothesis at the 5 per cent level of confidence. The data were reduced to 2 x 2 tables to eliminate cell frequencies of less than 5, and Yates correction was applied to compensate for cell frequencies of less than 50.

TABLE IV

INSOMNIA AND LENGTH OF STAY IN COUNTY HOME

(ITEMS IN WHICH CORRELATION WITH CONSTIPATION WAS FOUND TO BE STATISTICALLY SIGNIFICANT)

Insomnia and Length of Stay	Constipated	Non-constipated	? constipated	Grand Total	Statistical Evaluation	Level of confidence
Insomnia						
Yes	6	6	1	13		
No	11	40	2	53		
?		2	2	4	Chi^2	
Total	17	48	5	70	= 3.90	5%
Average length of stay in county home (in years)	5.31	9.48	11.2		t = 2.72	<1%
Mean age	75.6	74.1	76.2	75.2		

Item 12 (Table 3), "length of stay in the county home," shows $t = 2.72$ (Table 4). A "t" of 2.66 is significant at the 1 per cent level of confidence. Thus our $t = 2.72$ is significant above the 1 per cent level of confidence. In other words, the probability of a difference arising by chance alone is less than 1 in 100. The difference in length of stay of the constipated and non-constipated groups is therefore significant.

COMMENT

Almost without exception observers of gastro-intestinal conditions have been in agreement that constipation is a common symptom in advanced life.

Among 133 elderly private patients observed in Chicago, Portis and King (12) found 59 who suffered from either persistent or intermittent constipation or who used laxatives or enemas repeatedly. Sorter, Berg, and Necheles (13), summarizing their experience in the Home for Aged Jews in Chicago, the free clinics of Michael Reese Hospital, and with private patients, stated that ". . . constipation has been one of the most frequent complaints of people above 60 years of age and one of the most vexing problems therapeutically." This was also the experience of Wechsler, Kessler, and Goldsmith (14), and the opinion of Boas (15), Thewlis (16), and others. The reported frequency of constipation varied from 44 per cent (Portis and King) (17) to 25 per cent (Mueller-Deham and Rabson) (18). Monroe reports that among his investigated geriatric cases 22 per cent of the men and 33 per cent of the women were said to take cathartics or enemata every day or several times

each week (18a). Valdez (19) writes: "Constipation is the most frequent complaint of the aged."

The findings of the present survey indicate that constipation may prove to be far less frequent a phenomenon in old age than is generally assumed.

As far as frequency of physical complaints is concerned, constipation ranged behind many other symptoms. Table 5 shows that 8 items preceded it in frequency. In spite of the fact that arthritis and/or arthralgia appeared in a ratio of almost 2½ to 1, and fatigue, sight and hearing impairment, and urinary symptoms in a ratio of 1½ to 1, to constipation, there was a definite tendency on the part of the respondents to minimize these symptoms and a readiness to admit disturbances in defecation. This was evidenced when urinary symptoms were discussed. Many of the respondents felt that frequency of urination and pain in micturition are normal in old age and showed no concern about these symptoms; they were, however, worried about their bowel movement habits.

TABLE V

FREQUENCY OF OCCURRENCE OF SYMPTOMS IN ELDERLY COUNTY HOME RESIDENTS

Symptoms	Normal and mildly mentally ill		All groups	
	Number	Per cent	Number	Per cent
1. Pain in joints, limbs, and back	41	58.6	....	....
2. Fatigue	28	40.0	37	29.4
3. Sight: blind or poor	27	38.6	41	32.6
4. Hearing: deaf or poor	27	38.6	42	33.4
5. Micturition: pain and frequency	25	35.7	30	23.8
6. Dizziness	23	32.8	....	....
7. Crippled limbs	22	31.4	28	22.2
8. Headache	19	27.1	....	....
9. Constipation	17	24.3	22	17.4
Total number of subjects	70	100.0	126	100.0

This brings us to the question of the possible cause of constipation suggested by an analysis of our material. The statistical evaluation of the data correlating the various items with constipation was of great value. Neither physical disease, limitation of activity within the county home, nor other unfavorable factors proved to be statistically significant in these correlations. In other words, if we have assumed that sitting around doing nothing, being bedfast, suffering from physical invalidism, or being depressed and desperate might cause or be partially responsible for constipation in the elderly individual, there appears to be no statistical evidence to support this assumption. This does not mean that all the factors mentioned can be eliminated from etiological considerations. However, our statistical analysis shifts attention to other factors which seem to be more related to constipation than the commonly accepted ones. The present investigation indicates that psychological rather than somatic factors are most intimately related to constipation. Insomnia would appear to be one of the conditions that either cause constipation or is caused by the same factors that cause constipation.

Significantly, frequency of constipation was higher among those whose average residence in the county homes was of shorter rather than longer duration. To some extent this may be attributed to changes in habits caused by the elderly person's coming to the county home. However, changes in the aged person's habits are only part of the over-all extensive changes in his life. It takes time before the psychological and social factors of the county home resident's extramural experiences begin to fade away and he becomes conditioned to his new environment, which, although one of idleness, desperation, and petty irritations, is primarily one of finality as far as ambitions, aspirations, social position and new opportunities are concerned.

The difference between his intramural and his extramural experiences appears to account for the elderly resident's psychosomatic manifestations, constipation being one of them. This explanation is in contradiction to some reports concerning frequency of constipation among other institutionalized elderly persons. There is, however, a basic difference between the character of the previously reported institutional groups and those reported on here. The former consist of a predominantly urban population—residents of old age homes or hospitals situated in large cities. By virtue of the proximity of these institutions to the previous areas of the elderly resident's activity and to his relatives and friends, his ties to his extramural environment are probably sufficiently preserved so that they continue to be at least potentially an active psychological and social factor, influencing soma and mind in the habitual ways.

The subjects of this study had few ties with the outside world. A large percentage of them (94.4) were either single or had long been separated or widowed. Many of them had no relatives. The majority had spent most of their lives in farm districts and the county homes to which they were compelled to retire were usually far from the center of their former activities and they did not feel too strongly the attitudes and influences of their former environment.

A broader implication of this explanation is that to relate the problem of constipation in advanced life to age alone is not justified. It is probable that psychological factors, which play an important role in people of all age groups, are also of significance among the elderly. The apparent increase of constipation among certain groups of elderly individuals could easily be explained by the presence, in advanced life, of many more unfavorable factors than exist in the environment of younger age groups (20).

This survey indicates the need of further investigation in a similar direction. It is possible that large groups of elderly persons might be discovered in which constipation is not a problem. Sheldon writes, for example, "Faeces: habits were classed as normal in 421 cases, not ascertained in 55, and unsatisfactory in 1 subject only" (21). While our survey does not indicate, as does the Sheldon, that constipation in advanced life is not a problem, it does show that constipation among the investigated group is far less

a problem than in urban groups. It is to be expected that further study will clarify this question.

SUMMARY

(1) One hundred twenty-six elderly county home residents in the northwestern part of Iowa were interviewed. The data obtained were verified as far as possible by comparison with other data. The mean age of the group was 75.2, the oldest subject being 96 and the youngest 65 years of age. This paper reports findings concerning appetite and constipation.

(2) Appetite was found to be good or fair in 82 per cent of the subjects.

(3) Constipation was found in 17.4 per cent of all subjects and in 24.3 per cent of the non-psychotic and mildly mentally ill. In the latter group, however, only 17.1 per cent had less than one bowel movement per day, and only 12.9 per cent had to take laxatives.

(4) A statistical evaluation of the data obtained, particularly those concerning constipation, was possible since questions regarding digestive functions were included in the survey questionnaire, which was primarily directed toward investigating social and psychological aspects of elderly residents of county homes. It was found that correlations between constipation, insomnia, and length of stay in the county home were of statistical significance.

(5) An analysis of these findings is given. This study casts doubt on the widespread belief that poor appetite and constipation are major problems among elderly individuals. Further study is therefore advocated.

REFERENCES

1. Ginzberg, R., and Brinegar, W. C.: Psychiatric and Medical Aspects of a County Home Survey in Iowa, J. Amer. Geriat. Soc. 1:283-286, 1953.
2. Ginzberg, R. and Brinegar, W. C.: Psychiatric Problems in Elderly Residents of County Homes, Amer. J. Psychiat. 110:454-459, 1953.
3. Olsvary, V.: Psychological Aspects of a Survey of Elderly People in County Homes in Iowa, read at the 5th annual meeting of the Gerontological Society, Washington, D. C., September 5-7, 1952. Abstract in J. Geront., 7:489-490, 1952.

3a. Cavan, R. S., Burgess, E. W., Havighurst, R. J. and Goldhamer, H.: Personal Adjustment in Old Age, Chicago, Science Research Associates, Inc., 1949, Appendix A, pp. 149-159.

3b. Sheldon, J. H.: The Social Medicine of Old Age, London, Oxford University Press, 1948, Appendix 1, pp. 199-205.

4. Best, C. H. and Taylor, N. B.: The Physiological Basis of Medical Practice, Baltimore, Williams and Wilkins Co., 1950, pp. 604-605.
5. Ginzberg, R.: Nutrition in Geriatrics—Psychological and Somatic Aspects, Amer. J. Digest. Dis., 15:339-346, 1948.
6. Stieglitz, E. J.: Principles of Geriatric Medicine: Geriatric Medicine, Stieglitz, E. J., editor, 2nd edition, Philadelphia, W. B. Saunders Co., 1949, Chap. 2, p. 34.
7. Boas, E. P.: Treatment of the Patient Past Fifty, Chicago, Yearbook Publishers, Inc., 1944, p. 240.
8. Thewlis, M. W.: The Care of the Aged (Geriatrics), St. Louis, C. V. Mosby Co., 1946, p. 122.
9. Griffin, J. J.: Quasi-Institutional Care of the Aged, Geriatrics, 6:326-332, 1951.
10. Sheldon, J. H.: ibid., p. 52.
11. Dock, W.: Constipation and Diarrhea: Principles of Internal Medicine, Harrison, T. R., editor, New York, Blakiston Co., 1952, Chap. 16, p. 194.
12. Portis, S. A. and King, J. C.: The Gastro-intestinal Tract in the Aged, J.A.M.A. 148:1073-1079, 1952.
13. Sorter, H., Berg, M. and Necheles, H.: Constipation in the Aged, Attempt at Therapy, J. Geront., 4:121-126, 1949.
14. Wechsler, L., Kessler, L. A. and Goldsmith, M. L.: X-ray Study of Bowel Function in the Aged, Geriatrics, 6:293-297, 1951.
15. Boas, E. P.: ibid., p. 241.
16. Thewlis, M. W.: ibid., p. 79.
17. Portis, S. A. and King, J. C.: ibid.
18. Mueller-Deham, A. and Rabson, S. M.: Internal Medicine in Old Age, Baltimore, Williams and Wilkins Co., 1942 (Quoted from Portis and King, ibid.).

18a. Monroe, R. T.: Diseases in Old Age, Cambridge, Harvard University Press, 1951, p. 229.

19. Valdez, F. C.: Diseases of the Intestines: Geriatric Medicine, Stieglitz, E. J., editor, ibid., Chap. 34, p. 538.
20. Ginzberg, R.: The Negative Attitude Toward the Elderly, Geriatrics, 7:297-302, 1952.
21. Sheldon, J. H.: ibid., p. 112.

ABSTRACTS ON NUTRITION

PITNEY, W. R. AND BEARD, M. F.: *Serum and urine concentrations of vitamin B_{12} following oral administration of the vitamin.* J. Clin. Nutr., 2,2, Mar.-Apr. 1954, 89-96.

In both normal individuals and patients with pernicious anemia in relapse, serum concentrations of vitamin B_{12} show no significant alteration following the oral administration of 1000 γg. of the vitamin. When the dosage is increased to 5000 γg., serum concentrations in both groups are increased. In pernicious anemia, there is a correlation between hematological response and the demonstration of the vitamin in the serum following oral therapy. Vitamin B_{12} appears in the serum in combined form after adequate oral dosage. The absence of circulating free vitamin accounts for the failure to detect the increased urinary activity which is observed following parenteral therapy. There is a reduction of vitamin B_{12} concentration of the serum in pernicious anemia. The value of this test (for vit. B_{12} in serum) in determining which therapeutic agent to use in megaloblastic anemia is obvious.

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CHALMERS, J. N. M. AND HALL, Z. M.: *Treatment of pernicious anemia with oral vitamin B_{12} without known source of intrinsic factor.* Brit. Med. J., May 22, 1954, 1179-1181.

Cases of megaloblastic anaemia in relapse given single oral doses of 2,000-9,000 μg. of vitamin B_{12} showed initial haematological responses similar to those obtained by a single intramuscular injection of 20-100 μg. of the vitamin. Daily doses of 50 μg. of oral vitamin B_{12} taken when fasting caused significant haematological responses in cases of pernicious anaemia in relapse. A less satisfactory response was obtained when the same dose was taken with food.

The surface agent "Tween Twenty" did not appear to be of value in aiding absorption of vitamin B_{12}.

A case of pernicious anaemia in relapse has been initially treated and maintained in remission for over 18 months on a dose of 50 μg. of oral vitamin B_{12} taken daily on retiring at night. While intramuscular preparations are preferable and more convenient for routine management, it is concluded that, without intrinsic factor, oral vitamin B_{12} can be utilized when taken fasting by patients suffering from pernicious anaemia and that clinical and haematological remission can be obtained with oral vitamin B_{12} alone.

HARDINGE, M. G. AND STARE, F. J.: *Nutritional studies of vegetarians. 1. Nutritional, physical and laboratory studies.* J. of Clin. Nutrition, 2, 2, Mar.-April 1954, 73-82.

A comparative study of 112 vegetarian and 88 non-vegetarian adults, adolescents, and pregnant women is described. The results show that although the dietary intake of nutrients varied widely among individuals, the average intake of all groups, with the exception of the adolescent "pure" vegetarian, approximated or exceeded the amounts recommended by the National Research Council. Non-vegetarian adolescents consumed significantly more protein than did lacto-ovo-vegetarian and "pure" vegetarian adolescents. No evidence was obtained to indicate that a lacto-ovo-vegetarian diet failed to provide an adequate dietary for an expectant mother.

In general, measurements of height, weight, and blood pressures of these groups showed no significant differences. However, the "pure" vegetarians weighed appreciably less, an average of 20 pounds. Preconception and post partum weight gains and losses of the pregnant women were similar, as were the average birth weights of infants among the lacto-ovo-vegetarians and non-vegetarians.

The total protein, albumin, and globulin values, and the hematological findings for all the vegetarian and non-vegetarian groups were not statistically different.

HECKER, R. AND ANDREWS, W. H. H.: *Fat utilization in adults on a diet of cow's milk.* Brit. Med. J., May 15, 1954, 1131-32.

The authors placed themselves on exclusive diets of cow's milk for one month and felt no ill-effects. There was some flatulence and a tendency to constipation. During the last 3 days of the diet fat balances were carried out. It was found that 94 percent of the fat of milk was absorbed. As in infants, a considerable proportion of the excreted fat was *in the form of soap.*

WAGNER, S.: *Vitamin E in the treatment of dystrophic ulcers of the stomach.* Aerztl. Forsch. 8, 2, 51. Feb., 1954.

The dystrophic stomach ulcer in which serious metabolic disturbances give rise to a lowering of vitality of the stomach wall and thus lead to ulcer is to be sharply distinguished from the primary peptic ulcer in which the increased stomach activity is the ulcer inducing factor. The different ways in which it can lead to dystrophia are pointed out. The dystrophia primarily affects the muscular system and is manifested in creatinuria. Besides measures to regulate the metabolism of the muscles such as administration of prostigmine and glycocoll there are, above all, the sexual and adrenal cortex hormones which not only halt the creatinuria but also have the capacity to heal the stomach ulcer. The disadvantage of the hormone treatment lies in an early appearance of regressive development following a halting of the pituitary cells. The vitamin E in comparison shows a stimulation of the pituitary diencephalic system, whereby the mentioned metabolic disturbances are removed and vasodilatation and also capillary germination are obtained. The trophotropic effect of the tocopherols favors healing of the ulcer by removal of the metabolic damage without setbacks or other disadvantages.

Franz J. Lust.

MINOQUE, S. J.: *Alcoholism.* M. J. Australia, Mar. 6, 1954, 358-359.

Minoque, who has had extensive and continued experience with thousands of alcoholics, is finally convinced that alcoholism is a medical and not a psychiatric disease. Among the symptoms and signs, which have not been mentioned heretofore, he describes dryness of the skin, enlargement of the liver (not cirrhosis) as a reversible feature, the smell of acetone on the breath, the temporary improvement brought about by insulin or adrenal cortex, and the well known craving for sweets. He believes alcoholism is a physical disease about which at present we know almost nothing. It is a virgin field for investigation. Psychotherapeutic procedures, shock treatment and the use of Antabuse are really of no avail. "Without Divine help there is no adequate defence against that first drink" (A. A. literature).

HACKEDORN, H. M., CRAMPTON, J. A. AND PALMER, L. J.: *Intravenous glucose tolerance test in liver disease and diabetes mellitus.* Northwest Med., 53, 3, Mar. 1954, 257-262.

The intravenous glucose tolerance test was done on 6 normal young adults and 20 patients with abnormal carbohydrate metabolism in whom the disorder was not clearly recognized without the test. By combining the intravenous glucose tolerance test with liver function studies, the disordered carbohydrate metabolism of liver disease has been separated from diabetes in 15 cases, and in five cases both diseases were present. Following intravenous glucose, the rate of glucose degradation is reflected in the fall of serum inorganic phosphorus level. There is a relatively small fall in serum inorganic phosphorus in diabetics, but there is a moderate to profound fall in liver disease. Patients with both diseases have a fall within the low, normal range, and in addition, show an excessive glycosuria.

SEBRELL, W. H.: *Developing modern nutrition programs.* Public Health Reports, *69*, 3, Mar. 1954, *277-283.*

Modern nutrition programs promise a new era in public health. In most countries of the Western Hemisphere, including the U.S.A., malnutrition still is present. The use of vitamins has caused great improvement in morbidity from pellagra, beriberi, protein edema, macrocytic anemias and goiter. Kwashiorkor is a serious problem in some areas of the world, and in certain regions phrynoderma and ocular lesions prevail. Nutritional surveys still are very important, particularly in Latin America where diets frequently are inadequate in calories, and in vitamin A, riboflavine, and calcium. In Puerto Rico, two-thirds of the population subsist on diets clearly inadequate in some or all essentials. In regions raising chiefly non-food, commercial crops, education may be required for the introduction of even milk or yeast. In the U.S.A., obesity is our major nutritional problem and the use of appetite-depressants does not alter the deleterious dietary pattern. Pellagra is almost wiped out in the United States. Progress is being made in the fight against beriberi in the Philippines. Every nation today faces many needs relative to nutrition. Enrichment of bread and wheat flour is important. Governmental supervision is indispensable and education of the public very urgent.

MILLIS, J.: *The influence of nutrition on the growth rate in the first year of life of Chinese infants born in Singapore in 1951.* M. J. Australia, Feb. *27*, 1954, *322-327.*

57 male and 46 female "full-term, normal" Chinese infants of the lower income groups were studied throughout the first year of life. Breast feeding produced more rapid weight gain for the first 24 weeks than artificial feeding. The infants who were breast fed longer tended to be graded higher in the medical examination at the end of one year. Prior to the fifth month, such illnesses as occurred were chiefly in the artificially fed infants, but after the fifth month the morbidity increased rapidly. Most of the infants' diets were deficient in ascorbic acid, although no clinical signs appeared. At the end of a year, 31 percent of the infants had less than one pint of milk daily and were on diets deficient in high-grade protein, calcium, ascorbic acid and riboflavine.

COHEN, B. M.: *Diabetes mellitus among Indians of the American Southwest: Its prevalence and clinical characteristics in a hospitalized population.* Ann. Int. Med., 40, 3, March 1954, 588-599.

In two years in the hospital facilities of the Phoenix area of the Bureau of Indian Affairs, out of 16,296 consecutive admissions, there were 256 Indian diabetic admissions, an over-all case-admission rate of 1.5 per cent for the entire area. Diabetic coma did not occur. Obesity was common, the majority of patients presenting the "maturity-onset" type of diabetes. Diabetes increased in tuberculous patients. The prevalence of diabetes in this homogeneous group of Indians of the American Southwest lends strong support to Joslin's thesis of the universality of diabetes.

EDITORIALS

VEGETARIANISM

The writer of this editorial, presumably like most physicians, has always had an ill-defined contempt for vegetarianism. As some English physician expressed it, vegetarians are "full of self-righteousness and wind." However prejudiced one may be against an all-vegetable, or a lacto-ovo-vegetable diet, it appears that in all respects except weight, these people are the equals of their meat-eating friends. The recent report by Hardinge and Stare (1) indicated that blood proteins and blood counts were at just as good a level in non-meat-eaters as in those who enjoy cooked flesh of animals. In the case of "pure" vegetarians in their youth, the average intake fell a little short of the amounts recommended by The National Research Council. The pure vegetarians averaged 20 pounds less in weight than non-vegetarians. Further studies no doubt may deal with blood lipids and with resistance to infection in the two groups.

I know from experience that a vegetarian, for obvious reasons, is a very difficult person to entertain in one's home. As a matter of fact, a vegetarian ought never to permit himself to be a house guest anywhere. From experience, also, I have found in all the vegetarians I have met only two reasons for their restriction. The commonest reason is a semi-religious one. The other is merely that they do not *like* meat. I have very few vegetarians as patients but cannot decide whether this is due to the fact that they form a distinctly minority group or whether they are less prone to illness. Some time I would enjoy meeting a person who refrained from meat not because he did not like meat, and not because of some religious interdiction, but because he thought a vegetable or plant diet was better for him.

In the distant future we expect that, owing to dwindling meat supplies, populations will be forced to subsist largely on cereals, fruits and vegetables. It is comforting to know that, in some respects at least, such a diet will not prove harmful.

1. Hardinge, M. G. and Stare, F. J.: Nutritional studies of vegetarians. J. Clin. Nut., 2, 2, 1954.

MEDICINE AND THE LAY PRESS

Actually there is no good solution to the several problems arising from the lay reporting of medical news. One of the problems is that, with the exception of a very few "professional" writers, a somewhat distorted version of any given matter results. Seldom is this distortion due to misquotation of facts. It is due rather to the fact that the popular style of writing

fails to make distinctions which, however slight they may seem in themselves, cast an inaccurate character over the whole report. Not only so, but there is often introduced an almost emotional factor which certainly has no place in medical reporting. The net result is that patients, who, more and more, enjoy a "medical education," present themselves to the physician with preconceived ideas which render the task of diagnosis and treatment not only difficult but often quite distasteful.

It has been suggested in Switzerland that medical progress should not be called to the public's attention by the press but should be the subject of an official statement by the profession in order to eliminate "sensationalism." In the U.S.A., at least, there is no way to prevent lay reporting. For several years past, medicine has been "big news" and the public likes it. Time alone will smooth out the situation. The press will continue to use increasing caution with respect to the background of their professional medical writers. Finally, it is only fair to say that the writings of many of these professionals is much better and more accurate than some of the medical columns written by physicians.

BOOK REVIEWS

An Introduction to Bacterial Physiology. Evelyn L. Oginsky and Wayne W. Umbreit, W. H. Freeman & Company, San Francisco, California. 1954. $7.25.

The authors, who are associated with the Merck Institute for Therapeutic Research, unfold the inner workings of bacteria. Although the book is "technical" so far as the average physician is concerned, it is nevertheless very interesting. As in animal physiology, so in bacterial physiology, the essentials are expressed in chemical reactions, often of a complicated nature. Perhaps the one problem is no more difficult than the other.

Radiologie Clinique de L'intestin Grêle de l'adulte et de l'enfant. P. Porcher, P. Buffard and J. Sauvegrain. Masson et Cie, Paris. 5000 fr., 1954.

This volume of 614 pages with 350 figures (mostly x-ray reproductions) admirably exposes the many difficulties encountered in the examination of the small intestine. Various techniques are adequately described, and the abnormal appearances in various diseases and disorders are illustrated. Great emphasis is placed upon the examination of the small bowel in children. Thus far we have not had the pleasure of reading so complete a treatise on this subject of growing importance. The x-ray reproductions are particularly informative.

Handbook for Diabetic Children. Alfred E. Fische, M.D. and Dorothea L. Horstmann. Intercontinental Medical Book Corp., New York. 1954. $1.75.

The present volume is extremely satisfactory not only because it covers all that any patient with diabetes needs to know, but more particularly because it is written in simple language that children can understand. This is the only diabetic manual which we have seen that incorporates the latter feature.

The Meaning of Social Medicine. Iago Galdston, M.D. Harvard University Press, June 1, 1954. $2.75. (Published for the Commonwealth Fund.)

The reviewer has had the pleasure of talking with several professional persons with medical degrees who were enthusiastic about "social medicine," which, of course, must be distinguished from socialized medicine. Social medicine puts the emphasis on positive health, well-being, radiancy, buoyancy, etc., and naturally embraces a reasonable amount of psychology. The idea is not only to diagnose a disease and treat it intelligently, but to go further into the habits and associations of the patient, in order that he or she may, through practice, experience the more abundant life, physically, mentally, philosophically and even spiritually.

Galston's book is an able description of what social medicine might become and deserves careful reading. He feels that while present therapeutic medicine cannot engulf social medicine, the converse is not true. It all amounts to a widened definition of medicine and medical education, difficult as it may prove in practice. The enthusiasm of the "positive health" proponents is fairly contagious and after talking with them one feels that something very big has been contacted. Next day, however, it is quite obvious that what patients desire of us physicians is comfort and an end of suffering, and that in itself is an assignment. It is almost questionable if the medical profession ever could grasp the enthusiasm propounded. Furthermore, isn't positive health emphasis almost a specialty? Or is it something to be taken up by others, rather than by physicians?

Vitamin B_{12}. Selected Annotated Bibliography, 1954. Merck & Co., Inc., Rahway, N. J.

For those who are interested in the hemopoietic, growth and other potentialities of vitamin B_{12}, this 245 page book is extremely valuable, inasmuch as the whole literature of the subject is reviewed up to the present moment.

GENERAL ABSTRACTS OF CURRENT LITERATURE

ASTLEY, R. AND CARRE, I. J.: *Gastro-esophageal incompetence in children with special reference to minor degrees of partial thoracic stomach.* Radiology, 62, 3, March 1954, 351-362.

Short esophagus and a minor degree of thoracic stomach are not uncommon causes of vomiting in infancy. A reflux esophagitis may produce stricture of the esophagus in some cases. Roentgen diagnosis is not always easy and the recognition of thoracic stomach may require repeated examinations. The use of thickened feedings, and feeding the patient in a propped-up position are essentials in treating the infant so affected.

EANET, M. P.: *Serum hepatitis in recipients of irradiated human plasma.* Am. Pract. and Dig. of Treat., 5, 3, March 1954, 145-148.

A follow-up study of recipients of certain units of dried irradiated plasma prepared from reworked pools containing donations from 3,000 to 30,000 individuals was undertaken. Out of 27 recipients on whom follow-up studies were obtained, 3 cases of serum hepatitis and one probable case were found to have occurred. Attack rates for serum hepatitis in recipients of whole blood and in control hospital populations, which would include the occasional transmission of this disease by improperly sterilized syringes and needles, were less than 1 percent. Serum hepatitis should be considered a serious hazard in the administration of pooled plasma. Ultraviolet irradiation does not appear to have been successful in removing this hazard from the potentially infected pools studied. The use of large numbers of samples in the composition of plasma pools did not prevent hepatitis by diluting the virus below the point of infectivity.

HARRIS, H. I. AND PETERS, C. M.: *The treatment of psychosomatic disorders by the internist.* Am. Pract. & Dig. Treat., 5. 3, March 1954, 158-163.

Functional disease and disorder, based on the effects of emotion, are said to be present in 50 percent or more of patients consulting the internist. Primarily, the internist should remain an internist at all times but in these so-called psychosomatic disorders he can do much to help the ventilation by a sympathetic hearing of symptoms, in which he himself is careful not to obtrude his own personality.

DEMPSEY, W. S.: *Mobile left lobe of the liver.* Am. Pract. & Dig. Treat., 5, 4, April 1934, 287.

Two cases of right upper quadrant mass caused by mobile left lobe of the liver are reported. In each case a large, firm, freely movable mass was noted in the *right* upper quadrant. All diagnostic methods failed except laparotomy, when it was found that a mobile left liver lobe was lying on the right side of the abdomen. The author feels that the condition must be fairly common, although there was no mention of it in the Cumulative Index from 1927 through 1951. The condition might be expected following operation for diaphragmatic hernia, in which the supporting ligaments of the left lobe are cut.

BRUWER, A., BARGEN, J. A. AND KIERLAND, R. R.: *Surface pigmentation and generalized intestinal polyposis (Peutz-Jeghers syndrome).* Proc. Staff Meet. Mayo Clin., Mar. 24, 1954.

A case of the rare Peutz-Jeghers syndrome is described. Such cases present pigmentation of the skin and mucous membranes and have extensive colonic polyposis. Should a young adult present such pigmentation and complain of abdominal pain, cramping, obstruction and possibly rectal bleeding, it would seem that the diagnosis of generalized intestinal polyposis is almost certain. Fewer than 30 cases in which the lesion was proved have been described as yet.

RAWSON, H. D.: *Massive bowel resection following partial gastrectomy.* New Zealand Med. J., LII, 292, Dec. 1953, 496-499.

Seven days after a successful partial gastrectomy, a 62 year old man developed extensive intestinal gangrene, due, presumably, to a thrombosis of a portion of the superior mesenteric artery. Half the colon and all but 5 inches of the jejunum were removed. He made a good recovery with remarkably few symptoms, although his blood protein, calcium and potassium are low, and there is some edema of the legs, eight months after operation. The author has not been able to find in the literature a case of survival following so extensive a resection.

OGILVIE, SIR HENEAGE: *Abdominal emergencies.* New Zealand Med. J., XII, 292, Dec. 1953, 448-455.

With his usual insight and graphic manner of description, Ogilvie touches upon the many points of importance in the diagnosis and management of the "acute abdomen." Many of his statements are true aphorisms. Urgency is the chief characteristic of all abdominal emergencies and the problem of immediate operation one of utmost importance. He emphasizes the great *importance of inspection* of the patient and his abdomen. "Always listen to a doubtful abdomen." When no gurgle is heard over a period of 2 minutes, peritonitis is present. Tenderness elicited by rectal digital examination also indicates peritonitis. Acute appendicitis and acute right pyelitis in little girls are frequently difficult to differentiate. To make a positive diagnosis of appendicitis is permissible, but one should not particularize about the position or pathological state of the appendix because he is very likely to be wrong.

COHEN, S. G. AND STAPINSKI, S. M.: *Enteritis and urticaria associated with trichomonas hominis*

infection. Am. Pract. & Dig. Treat., 5, 4, Apr. 1954, 238-9.

A case is reported, the important aspects of which suggest that enteritis and urticaria may be causally related to trichomonis hominis infection of the intestinal tract. The intestinal parasite was successfully eradicated following a course of aureomycin therapy.

TREVATHAN, R. D.: *Primary carcinoma of the liver.* Am. Pract. & Dig. Treat., 5, 4, 272-275.

Primary hepatic cancer is uncommon but not rare. Two cases are described, the first developing on the basis of a cirrhosis of the liver. The second case had the presenting symptoms of a spinal cord tumor, and diagnosis was made at post-morten. Cirrhosis is usually the precursor of the disease. Intraheptic as well as extrahepatic metastases are common. The clinical findings suggest cirrhosis, but there is a rapid downhill course and usually some palpable nodules in the liver. The only hope of cure is surgical eradication early, and this seldom is possible.

BROWN, C. H. AND SIMS, J. R.: *Regional enteritis involving the duodenum. (Report of 2 cases).* Cleveland Clin. Quart., 21, 2, April 1954, 95-102.

Two cases of regional enteritis involving the duodenum are presented. Such involvement is so rare that only 13 such cases have been previously reported. Both were relieved by side-tracking operations, a duodenojejunostomy in one and a gastrojejunostomy in the other. The first operation is preferable when almost complete obstruction of the duodenum is present as it permits a better mixing of acid stomach juice with the bile, without regurgitation into the stomach and rather obviates marginal ulcer. Such patients as these are likely to be suspected of functional indigestion until x-ray studies have been made. Regional enteritis should always be considered as a possibility in obstructing lesions of the duodenum.

HIRSCH, E. F.: *Symptomless carcinoma of the cardia of the stomach.* Ill. Med. J., 105, 4, 1954, 195-197.

A white male aged 55 presented with a mass in the left side of the neck, biopsy of which revealed squamous cell carcinoma. He developed pain in one thigh and here a nodule of the same kind was found. Esophagoscopy and x-ray were used in an effort to find the primary neoplasm, but not until autopsy was it found—a diffusely infiltrative carcinoma of the cardia of the stomach which had produced no symptoms of any kind.

MATHEWS, F. J. C.: *Enteric pneumatosis.* Brit. Med. J., April 10, 1954, 851-852.

Enteric pneumatosis is a condition in which the intestinal lymphatics become blocked and distended by gas, producing multiple gas cysts both subserous and submucous in position. It occurs chiefly in men between the ages of 30 and 50, is accompanied by vague digestive symptoms, and would appear to be subject to spontaneous resolution. The most likely complication is intestinal obstruction. In a reported case, the cysts were seen both proctoscopically and by barium enema. The patient was led to consult the doctor because of bloody stools. The distal colon was excised.

BOYCE, F. F.: *The role of atypical disease in the continuing mortality of acute appendicitis.* Ann. Int. Med., 40, 4, April 1954, 669-693.

The mortality from acute appendicits has fallen decisively in the last 25 years and especially in the last several years, but yet 2600 persons die of the disease annually in the U.S.A. One reason for the continuing mortality is the idea that an appendiceal abscess is harmless. Above all, it should be remembered that the symptoms and signs are atypical in 25 percent of cases. Antibiotic therapy alters the picture. The public has been given the erroneous impression that appendicitis today is harmless. Furthermore, important medical journals are not using their influence to teach the continuing hazard of this disease.

MACDOUGALL, I. P. M.: *Ulcerative colitis and carcinoma of the large intestine.* Brit. Med. J., April 10, 1954, 852-854.

MacDougall describes 5 cases of colonic cancer found among 126 cases of ulcerative colitis. He feels that the risk of cancer of the colon in persons suffering from ulcerative colitis is at least 5 times as great as that for the general population. It seems that the longer the colitis continues, the greater is the risk of cancer.

LONG, J. C., JR.: *Nonparasitic cyst of the liver.* Texas State J. M., 50, 4, April 1954, 253-255.

Long discovered a smooth soft tumor attached to the right liver lobe in a woman of 55 who had applied because of a gynecological condition. External marsupialization was performed and Zenker's solution was injected into the cyst cavity twice weekly beginning about 2 weeks after the operation. A perfect result was obtained. This was one of the largest nonparasitic cysts ever reported, measuring 18 by 14 by 12 cm. Marsupialization is the operation of choice when the cyst cannot be actually removed.

ROSE, T. F.: *Perforated peptic ulcer at the Royal North Shore Hospital of Sydney from Sept. 1949 to June 1953.* Med. J. Australia, Feb. 13, 1954, 240-243.

Sixty-two patients were admitted to hospital during the years indicated with perforated peptic ulcers. Six of them were treated by aspiration therapy with 3 deaths, two received no treatment and one died, and 54 patients were treated by conservative operation of suture with only one fatality. The best treatment for perforated ulcer appears to be that of suture of the ulcer with adequate follow up. Aspiration therapy is too hazardous. Emergency gastrectomy has only a limited place in the therapy of perforation.

SALEMBIER, Y.: *Functional disturbances of common biliary duct. (Sphincter of Oddi excluded.)* Arch. mal. App. dig. T. 43. No. 1, January 1954, p. 42.

This work is based upon cholangiographic pictures made on 8 patients. 4 cases of hypotonia and 4 of hypertonia are presented.

The diagnosis can be determined only in very precise circumstances. Passive dilatations of the biliary tract above an obstacle of Oddi's sphincter (hyper-

tonia or sclerosis) must be chiefly suppressed in this study. It's necessary to support the diagnosis upon the rate of pressure of the common duct: low in hypotonia, generally high in hypertonia.

All the cases concern operated patients and consequently in all of them, it has been possible to suppress every organic participation liable to explain any compression or broadening of the biliary duct. But these functional disorders are practically always discovered in an organic syndrome nearly always caused by the gallbadder.

The syndromes of hypotonia generally concern the whole biliary duct whereas hypertonia chiefly appears as spasms limited to a part of the biliary duct corresponding to the pictures presented by Mirizzi as early as 1938.

The author has thought of supporting his cholangiographic statements which would show motivity of the common duct by an anatomic and physiological argumentation.

Besides its own innervation, the biliary duct offers a musculature which, according to the sections (sections made at different stages on 8 corpses) appears as placed in 2 strata, one longitudinal discontinuous, and around this one are circular muscular fibers.

The physiological study made on the common duct taken out of the guinea pig has always shown a contraction for a solution of acetycholine (2 x 10 - 6). Decontraction was obtained with a solution of Theophylline Ethylene diamine.

Mirizzi draws therapeutic conclusions from these syndromes when they are connected with disturbances of Oddi's sphincter. It is difficult to propose treatments aiming at medical or surgical cutting of the sympathetic in case of hypotonia and of the Vagus in case of hypertonia.

Therefore the study of the cholangiographic pictures presented shows disturbances which appear only in the common biliary duct. This duct must have its functional autonomy and what has been aimed at in this work was to prove it once more by clinical, anatomic and experimental arguments.

LEVY, MAX AND LAPIR, M.: *Variation of the post-operative calcium.* Arch. Mal. App. Dig., T. 43, No. 1, January 1954, p. 58.

The physiologists Benedict, G. Lusk, Cathcast, Herman, etc., have, in the course of a thorough, long-duration water-diet, carefully studied the variations of calciuria in man; they demonstrated that—roughly speaking—nine-tenths of the lost calcium *comes from the bones.* The daily calcium is important during those 20 to 30 days of such experimental fasting.

The water-diet is not the only circumstance apt to bring about an increase of calciuria; bed-confinement increases azoturia, and it may even double calciuria, and fecal calcium augments by one-third. A bone fracture, with confinement, magnifies such effects. The evolutionary crisis of diabetes, with acidosis evinces still more marked actions.

Despite the magnitude in the research work referring to the post-operative electrolytic perturbations, there practically exist no documents concerning calciuria.

The authors study it in the case of 58 operated patients in the course of the first 2 to 6 days following the operation when there practically exists no food supply and when there is no motion of the bowels.

Those subjects received on this day of the operation:

1 liter of salted physiological serum and subcutaneous 500 cubic centimeters of salted serum 4 per cent (20 g).

Then 30 gr. of the same serum distributed between the first and second day following the operation in intra-venous injections, a treatment which, in nearly all cases, annuls nitrogen post-operation disassimilation.

Urinary nitrogen and calcium were noted every day, which allowed us to know which part of calcium came from soft tissues of catabolised proteid nature and which from osseous tissues.

The data then gathered show:

1) The variability of the calciuria during 24 hours. The least is 21 mg, the most important 816 mg (average calciuria of the subject on ordinary mixed diet being 200 to 300 mg).

2) The considerable usual importance of calciuria with a bone origin.

3) The fact that age has no influence upon this phenomenon. An old person (78) had nitrogenous and calcic losses which appeared as the smallest among all those noted.

4) The absence of any relation between azoturia and calciuria: for the same loss of nitrogen the destruction of calcium may vary from 1 to 10.

5) The variations of calciuria from one day to the other.

6) The absence of any relation between pre- and post-operative calciuria.

BUTTIAUX R. AND MORIAMEZ, J.: *Occurrence and polymorphism of Shigella Sonnei infections.* Arch. Mal. App. digestif. T. 42, No. 12. Dec. 1953, p. 1360.

In 1949, authors reported on the ever greater occurrence of Shigella sonnei in Northern France. It is confirmed by this study carried out in 1951, 1952, 1953. Authors did not find Sh. dysenteriae 1 and 2 any more, Sh. flexneri and Sh. boydii very rarely. Out of 89 Shigella isolated, Sh. sonnei was identified 84 times.

Sh. sonnei can produce three main clinical manifestations:

1—acute dysenteriform syndrome (25%);

2—food intoxication (17.8%). Authors describe an intoxication by this germ in a college. 120 teachers and students were affected. The cook was a carrier;

3—subacute or chronic diarrhoea (51.7%). It is the more important manifestation and its origin is very often mistaken. Diagnosis is made by bacteriological examination of stools, which must be performed in all cases even when microbic origin is not suspected. Sero-agglutination (even with phase I) does not often give useful information.

DELANNOY, E. AND PARIS, J.: *Enormous abdominal colloid cancer six years after colectomy for cancer.* Arch. Mal. App. Dig., T. 42, No. 12. Dec. 1953, p. 1375.

E. Delannoy and J. Paris (Lille) report the case of

a male 57 years old who had had six years before a resection for carcinoma of the left colon. At admission was found an enormous abdominal tumor; it occurred suddenly eighteen months before, following a painful episode of the right superior abdomen.

Several similar episodes occurred in the same manner followed every time by a growth of the tumor. However, the patient's condition remained very good, allowing normal activity except for the presence of a few dyspeptic symptoms. The abdomen was extremely distended, surface was irregular, consistency variable with hard zones at some other points. The abdominal mass was mobile with respiratory movements. The percussion showed sonority around the tumor. No ascites nor jaundice. Routine laboratory data were at normal levels.

The most probable diagnosis was metastatic carcinoma of the liver; however, the sudden appearance, the long duration of the disease, the excellent condition of the patient, the negativity of hepatic tests, led them to consider another possibility like pancreatic cyst.

Laparotomy: Very important tumor of bluish appearance looking like an ovarian cyst. Puncture evacuated a dirty liquid content of about 4 liters. Blunt dissection allowed them to separate a very elongated gallbladder and transverse colon. Dissection was more difficult along the greater curvature of stomach. There was no vascular pedicle, nor adhesions to other abdominal viscera. The tumor weighed 3 Kgs. without its liquid content. Postoperative course uneventful. The patient was found in excellent condition after 10 months.

Histologic examination showed a colloid epithelioma, probably from intestinal origin.

The authors believe that it is an important metastatic lesion (7 Kgs 500) from the primitive cancer, developed in a lymph node of the greater curvature. They insist on the rarity of such enormous metastatic lymph node lesions which it is possible to remove despite the clinical appearance of inoperability.

ALBOT, G., KAPANDJI M. AND DRESSLER, M. *An assay of the physiopathology of timed intubation of the duodenum. 1. Concerning the role of the duodenum in certain anomalies and in particular that of the time of the closure of the Oddi and of the bile B.* Arch. Mal. App. Dig. T. 43, No. 1, 1954, p. 5.

G. Albot, Kapandji and Dressler bring evidence showing the role played by the duodenum in the prolongation of the closure period of the Oddi sphincter and in anomalies of the flow of the bile B and their evidence is likely to cause a revision of the physiopathology of duodenal intubation.

The case in question was that of a woman suffering from painful attacks in the right hypochondrium and to whom were administered one after the other 2 cholecystographies, 2 timed duodenal intubations, 1 timed cholecystographic intubation and a per- and post-operatory biliary radiomanometry. The cholecystography showed a hyperkinetic gall-bladder emptying to 75% and the biliary radiomanometry enabled the existence of irritation of the gallbladder with feeble spasms of the cystic and of the Oddi sphincter to be diagnosed.

Timed intubation of the duodenum on the other hand, interpreted by the usual standards, would have suggested dyskinesia of the cystic with hypertension of the Oddi sphincter: during the intubation there was observed a 10 minute period of closure of the Oddi sphincter giving way after ingestion of novocaine which brings on an immediate flow of hyperconcentrated bile B; a second intubation was marked by a 10 minute phase during which the Oddi sphincter was closed, a prolonged vesicular phase of 45 minutes with hyperconcentrated bile B.

Now cholecystographic intubation has enabled the apparent contradiction existing between cholecystography and radiomanometry on the one hand and timed intubation on the other to be resolved.

Considering cholecystographic intubation without the radiographic exposures made during its course, results were noted comparable to the previous intubations, the Oddi sphincter closed for 20 minutes, followed by a very long vesicular phase of 65 minutes with interrupted flow, a period during which there was pain in the right side of the hypochondrium.

If this same intubation were interpreted in the light of exposures made during its administration it would be noted:

1) that during the period that the Oddi sphincter is closed for an abnormal length of time (20 minutes) the volume of the gall-bladder diminished from 18 to 15 cm^3, that the cystic and the choledochus became suffused and bile from the gall-bladder colored with Telepac passed into the duodenum 10 minutes after the beginning of the closed Oddi phase, but that this bile was only visible in the upper portion of the duodenum and was not in contact with the bulge in the probe.

2) that during this time there existed a medio-duodenal spasm, as could be deduced from the fact that the part of the probe in the second portion of the duodenum came near the vertebral column becoming rectilinear instead of concave, and that the bile accumulated in the proximal superior pouch of the second part of the duodenum without coming into contact with the bulge of the probe in the distal pouch at the genu inferius.

3) that the gall-bladder became invisible and consequently almost empty 15 minutes after the beginning of the vesicular phase whilst the flow of bile B through the probe was prolonged for 65 minutes. It may thereby be concluded that in reality the emptying of the gall-bladder was very much more rapid than the intubation led one to suppose; the flow which followed the radiological emptying of the gall-bladder was that of the bile B stored in the proximal pouch of the duodenum and mixed with the hepatic bile which arrived in the distal pouch after reduction of the medio-duodenal spasm.

4) that furthermore, the interruption of the flow of bile was not necessarily the result of disturbances of the contraction and emptying of the gall-bladder since this irregularity in the flow

was produced during the evacuation of the bile stored in the duodenum.

The authors conclude that in timed duodenal intubation the role of the duodenum is likely to modify completely the significance of the results of the intubation. They believe it necessary to carry out timed intubation of the duodenum with the help of a double coupled probe whose end openings correspond respectively with each of the two duodenal pouches in case of medio-duodenal spasm.

NIEMGEERS, L. AND MAERMAN, J.: *Cholecystocholangiography with Biligrafin.* Acta Gastro. Belgica 17, 1, 38. Jan. 1954.

The authors report 25 non-selected cases of cholecysto- cholangiography with biligrafin. No visualization at all, in two cases; in two other cases the gallbladder was excluded by the peroral method. By the new drug a very good cholangio-cholecystography was obtained. A good cholecysto-cholangiography was obtained in 22 out of 25 cases. (88%). Perfect visualization was performed in all five cholecystectomised patients. Those numbers correspond to Hagedorn's statistics. The biggest advantage of the new drug is the short visualization time (time between the administration and the visualization of the bile ducts). Darker contrast of the cholangiography films, even after cholecystectomy.

Franz J. Lust.

DEMEULENAERE, L. AND WIEME, R. J.: *Cortisone, methylandrostenediol and liver.* Acta Gastroenter. Belgica 17, 1, 16. Jan. '54.

Prolonged administration of methylandrostenediol (5-10 mg pro die) plus cortisone (5-10 mg pro die or 5 mg twice a week) is compared with administration of the same doses of Cortisone alone.

Cortisone necrotising action on liver tissue is inhibited by methylandrostenediol, and evidence of growing collagen tissue is given by Mallory's technic. There are cylinders in the bile canaliculi. Flocculation and turbidity tests are equal in both cases. Proteinaemia remains normal. Electrophoresis shows the same important troubles of the protein metabolism, especially the supplementary fraction alpha 3. On the contrary, the rate of albumin fraction is higher, and the gamma fraction, though lower, never disappears. It is concluded that the antagonism between methylandrostenediol and cortisone is not a mathematical one, speaking of protein catabolism. It must be underlined that methylandrostenediol impairs bile excretion in the liver tissue.

Franz J. Lust.

CATTAN, R., FRUMUSAN, P. AND BUCAILLE, M.: *Pre-frontal infiltration of novocain in the pathology of the digestive system.* Arch. Mal. App. Dig. T. 43, 2, Feb. 1954.

In the hope of bringing relief to sufferers from incurable cancers, M. Bucaille perfected two years ago a method which, by using special apparatus and exact radiological location, enables a very tiny portion of the prefrontal lobe to be infiltrated. The substance used is a 1% solution of novocain.

The authors have used this method in three cases of very serious digestive hemorrhage and in one of gastric ulcer. Hemorrhage was due in the first case to a diverticulosis of the sigmoid flexure in a patient suffering from progressive rheumatoid arthritis, and in the second to an ulcerative recto-colitis, in the third to a latent duodenal ulcer. In the three cases, infiltration caused an immediate cessation of the hemorrhage. Furthermore, the progressive rheumatoid arthritis of the first patient was considerably improved. The very serious attack of ulcerative colitis was mitigated but there was a relapse, benign in nature however, a few months later.

The gastric ulcer was an outsize ulcer of the lesser curvature in an old man. Very varied medical treatments which had been tried for three months had failed to relieve the intolerable pains. Bilateral infiltration of the pre-frontal lobe caused the immediate disappearance of pain and a rapid cure of the niche.

The authors discuss the working of the method which cuts, by dilaceration, the fibers leading from the frontal cortex to the thalamus. The grey matter being hardly touched, no personality change nor any of the disadvantages of lobotomy are observed. These cases throw new light on the well-known action of psychism in some affections of the digestive tract. These should be studied together with the psychosomatic and cortico-visceral theories at present held in various countries.

OKADA, R.: *Experimental studies on the pathogenesis of non-specific localized enteritis.* Nagoya Med. J., 1, 3, 193. July 1954.

The ileum of the rabbit tested with coli filtrate, and celomic fluid and extract of ascaris showed positive Shwartzman phenomenon. Further the reaction resembled the acute forms of non-specific localized enteritis.

B. coli is found universally in the intestine and ascariasis is very common among oriental people. Hence it is natural that in the intestine there exist the active principles of Shwartzman phenomenon. When the active principles are absorbed through the intestinal wall, the intestine is in a preparatory state for Shwartzman phenomenon. In ascariasis, the mucosa is injured by the ascaris, and the absorption is made easier. When the active principles of the B. coli and the ascaris are absorbed into the blood stream, Shwartzman phenomenon, in other words non-specific localized enteritis, will result. Further, in Shwartzman phenomenon, the allergic antigen antibody reaction acts as provocative injection, and hence, it is conceivable that the cause of this disease is rendered clearer.

Franz J. Lust.

OCCY-CRYSTINE CONTINUES AS SALINE-CHOLAGOGUE STAND-BY IN CONSTIPATION

For over 30 years a great number of physicians have prescribed Occy-Crystine for rapid, gentle, thorough relief from functional constipation. This saline-cholagogue hypertonic solution of polysulfides acts two ways to combat intestinal sluggishness.

Occy-Crystine provides (1) the "liquid bulk" via saline action, for smooth, gentle, thorough elimination of intestinal waste, and (2) a richer flow of natural, physiologic laxative bile. Occy-Crystine relieves constipation and its distressing symptoms—fatigue, headache, gas distention, bloating, etc. It is particularly useful in constipation in the aged, the obese, arthritic, bedridden, and bland diet patients.

Gentle diuresis is another attribute of Occy-Crystine which is valuable in certain arthritic, obese and other patients who may find increased urinary output helpful. And Occy-Crystine makes available colloidal sulfur which it precipitates upon contact with gastric hydrochloric acid. Available in 4 oz. and 8 oz. bottles. Samples and literature upon request from Occy-Crystine Laboratory, Salisbury, Connecticut.

PRIMAQUINE SHARPLY CUTS MALARIAL RELAPSE RATE IN RETURNING KOREAN VETS

Mass therapy with the antimalarial primaquine of more than 300,000 troops returning to the United States from Korea aboard ships resulted in a "material reduction" in the number of relapses from Korean vivax malaria, according to Dr. Charles P. Archambeault, medical director, Sea Transport Service, U. S. Navy.

His report on the comprehensive ship-board study conducted with American troops from 1951 through 1953 is published in the Journal of the *American Medical Association* (154:1411, April 24, 1954).

During this period all United Nations armed forces in Korea used Aralen (chloroquine) routinely, the author states, adding "it is an excellent drug for the suppression of malaria." He attributes the "superior combat efficiency of U. N. troops" to use of the drug. Purpose of administering primaquine to returning servicemen was to cut down the incidence of vivax relapses.

Of the 415,340 troops returned by ship to the U. S. between August 1952 and December 1953, a total of 332,925 completed the 14-day course of treatment with primaquine. The remainder failed to complete the full course because some ships made the voyage in less than two weeks, the report says. Less than 20 men were removed from primaquine treatment during the voyages as the result of motion sickness.

"There were surprisingly few toxic reactions," Dr. Archambeault notes.

Only 1,060 cases of relapses from Korean vivax malaria were observed among military personnel on active duty in the U. S. during the first six months of 1953. By that time, more than 600,000 veterans had returned from Korea. This compares with 11,795 relapses in this country between July and December 1951, when only 183,000 troops had been returned.

After 17 months' operation of the mass primaquine therapy program at sea, the article says "a material reduction in the number of relapses occurring in the United States was demonstrated."

Aralen and primaquine are manufactured by Winthrop-Stearns Inc.

DR. IVOR GRIFFITH RECEIVES PORTRAIT FROM WYETH LABORATORIES

Presentation of an oil painting of Dr. Ivor Griffith, president and dean of the Philadelphia College of Pharmacy and Science, was made to Dr. Griffith at the annual alumni dinner of the College by Philip H. Van Itallie, editor of the Pulse of Pharmacy, published by Wyeth Laboratories.

The oil portrait executed by Dr. Furman J. Finck, professor of painting at the Tyler School of Fine Arts, Temple University, is the first in a series of cover paintings of deans of pharmacy commissioned by Wyeth from Dr. Finck. The portrait of Dr. Griffith will appear on the cover of the June issue of Pulse of Pharmacy which is distributed to pharmacists throughout the nation by Wyeth.

Dr. Griffith has been dean, president and research director of the Philadelphia College of Pharmacy and Science since 1941. This popular dean with a lifelong background in pharmacy and organic chemistry has also contributed greatly to the humanities. He wrote two collections of poetry and prose under the titles of "To the Lilacs" and "Lobscows." He also organizes Welsh songfests, collects driftwood and raises flowers. For 20 years he edited the American Journal of Pharmacy.

The dinner was held in honor of the graduating class of the College and was attended by alumni, faculty members and members of the Board of Trustees.

PARKE, DAVIS & COMPANY FORMALLY OPENS NEW MANUFACTURING LABORATORY IN INDIA

Bombay, India, July 8.—Medical and civic leaders of India joined with Parke, Davis & Company today in formally opening the firm's new manufacturing laboratory here.

Featured were a luncheon and plant tour for approximately 40 representatives of the city and national governments and the medical and pharmaceutical professions. Included were Raj Kumair Amrit Kaur, Indian Minister for Health; Shantilal H. Shah, Bombay Minister for Labor and Public Health; and Dr. Jal Patel, honorary surgeon to the President of the Indian Union.

Attending from Detroit was E. S. Bauer of Parke-Davis' Overseas Division.

A message from W. R. Jeeves, vice president and director of overseas operations, hailed the opening of the Bombay plant as "exceedingly significant."

He said, "This is an initial project with which to gain manufacturing experience in India, to serve as our guide when the time comes to decide on a series of extensions of the present manufacturing facilities."

Jeeves added that the new Parke-Davis project "is evidence of our faith and confidence in the future of India."

Parke-Davis set up its first India branch office in 1899 at Simla and moved to Bombay in 1907.

The new manufacturing facilities are located on Forjett Street in a leased building which has been extensively remodeled during the past year.

The three-story structure, with approximately 15,000 square feet of space, is partially air-conditioned for special low-humidity manufacturing.

Located in the northwest section of Bombay, the new laboratory will manufacture a full-line of basic Parke-Davis products to meet the requirements of the Indian medical and pharmaceutical professions.

Approximately 80 will be employed in the new facilities, Jeeves said.

The reinforced concrete and brick building also will house a lunchroom, quality control laboratory and bonded manufacturing and warehouse section as required by Indian law for alcoholic preparations.

This is the third Overseas laboratory opened by Parke-Davis during the last two years, making a total of nine manufacturing units operated by the company abroad.

Architect for the remodeling was F. McKnight of Bombay, while the general contractor was the Sewri Engineering Company, also of Bombay.

W. G. Lloyd is the company's general manager in Bombay, with Walter Davies in charge of manufacturing and Dr. A. N. Rao as manager of quality control.

LACK OF VITAMIN C IN OLDER PATIENTS

Clinical studies of aged hospitalized patients reveal definite tendencies toward a decline in blood concentration of Vitamin C, Dr. J. E. Kirk, Washington University School of Medicine, said in a symposium on gerontology conducted recently by the School of Public Health, Johns Hopkins University. (Source: N.A.R.D. Journal, May 17, 1954, p. 10.)

MOTHERS WHO LOSE BABIES MAY BE "EASY BLEEDERS"

A tendency to bleed too easily, whether manifested by nosebleeds, bleeding gums or skin that bruises readily, often means a Vitamin C deficiency. Easy bleeding was common among 2,000 women who had lost one or more babies, Dr. Carl T. Javert, Cornell University Medical College, reports. One role of Vitamin C is to provide the binding material that reinforces the walls of the small blood vessels or capillaries. "A distinct correlation was found between Vitamin C deficiency and decidual hemorrhage," says Dr. Javert. In this condition, there is bleeding of the vessels in the lining of the uterus during pregnancy. Treatment, as outlined by Dr. Javert, includes a diet rich in citrus fruits. (Source: "Studies on Spontaneous and Habitual Abortion in Relation to Vitamin C Deficiency," presented at Conference on Research in Medicine and Nutrition, Florida Citrus Commission, Lakeland, Florida, March 11, 1954. Full paper on request.)

AGES 13 AND 14 "ROCK BOTTOM" FOR VITAMIN C

Boys and girls 13 and 14 years old "hit rock bottom" in Vitamin C intake, according to Dr. Pauline Beery Mack, research nutritionist and dean of College of Household Arts and Sciences, Texas State College for Women.

Dr. Mack reported on her survey of the food intake of 2,550 children and teen-agers and 2,200 adults at a recent Conference on Research in Nutrition and Medicine arranged by the Florida Citrus Commission.

Not a single boy of the 13-14 age group consumed enough Vitamin C, necessary in tooth formation, bone growth, and maintenance of the gums and blood vessel walls in proper condition. Only one girl in four came up to par. Dr. Mack recommends that teen-agers, when snacking between meals, drink orange juice, since it provides sugar for energy plus Vitamin C. (Source: "Studies of Nutrition and Fatigue in Adults, Teen-Agers and Younger Children" by Pauline Beery Mack, Ph.D., Sc.D., Dean, College of Household Arts and Sciences, Texas State College for Women, presented at Conference on Research in Medicine and Nutrition, Florida Citrus Commission, Lakeland, Florida, March 12, 1954. Full paper on request.)

CITRUS FRUIT AS A TOOTHBRUSH

Detergent fruits are nature's toothbrushes, states "Diet and Dental Health," the new booklet published by the American Dental Association.

"Mentioned as outstanding among these detergent foods are fruits, such as oranges, grapefruit and apples, and raw vegetables, such as celery and carrots. The booklet advises: "Foods that require thorough mastication, during which they literally sweep over the teeth, between the teeth and over all the soft tissues, cleansing them and stimulating them are called detergent foods. . . . In addition to toothbrushing, every person should include in his diet, particularly at the end of each meal, some detergent food such as a citrus fruit."

AUSTRALIAN REPORTS 40-90% OF AIRSICKNESS CAN BE PREVENTED WITH BENACINE

Sydney, Australia.—Airsickness is a physiological response, not all psychological, Dr. J. C. Lane reported in The Medical Journal of Australia (Vol. 1:465, 1954).

"In my opinion," he wrote, "the medication of choice is the administration of 'Benadryl' (hydrochloride), 25 milligrammes, with hyoscine (hydrobromide), 0.33 milligramme. This combination (known commercially as "Benacine") will prevent airsickness in 40% to 90% of air travellers who otherwise would be sick."

At certain times of the year and on certain routes, airsickness is a "very real drawback" to air travel in Australia, he added. On inland routes in the summer, when aircraft repeatedly have to climb and descend through turbulence extending as high as 9,000 feet, the airsickness rate is high.

"Airsickness is preventible: why not prevent it?" Dr. Lane asked.

CHOLOGRAFIN

A new product which will make x-ray visualization of the bile ducts possible in most cases where such examination has heretofore been difficult or unsuccessful, is being released by E. R. Squibb & Sons. Named Cholografin, the Squibb contrast medium is a water solution of a crystalline substance which is excreted relatively preferentially by the liver. Its excretion is rapid enough and the concentration sufficient to give a high degree of

visibility under x-rays. It is administered by intravenous injection.

Cholografin is unique in that it permits non-surgical examination of bile ducts both in patients with intact gallbladder and in those in whom the gallbladder has been removed. In cases where the gallbladder is intact but lacks concentrating power, sufficiently high concentrations of the compound are obtained in the biliary ducts to permit x-ray study within 20 to 25 minutes following injection. Such concentrations may reach 30 to 100 times those seen in the blood. Within an hour after injection, filling of the gallbladder begins. Since Cholografin does not depend on the concentrating power of the gallbladder, maximum concentrations of Cholografin are detected in this organ in from two to two and a half hours even when oral preparations fail.

Well tolerated, Cholografin may be employed in patients who cannot take contrast media orally. Where results obtained with the use of the oral media are unsatisfactory, the patients may be re-examined the same day with Cholografin. Administration of the Squibb contrast medium is simple and reliable. It avoids the possibility of patients failing to take the required dosage of oral medium at home, and the further possibility of variation in the amounts of oral contrast medium absorbed through the digestive tracts of different patients.

Cholografin is supplied by Squibb as a 20 per cent sterile aqueous solution in ampules of 20 cc.

AMERICAN COLLEGE OF PHYSICIANS TO USE NATIONWIDE TV CLOSED CIRCUIT TELECAST IN CONNECTION WITH ITS POST-GRADUATE PROGRAM

On Thursday evening, September 23, 1954, from 6:00 P. M. to 7:00 P. M., Eastern Daylight Saving Time, the American College of Physicians will utilize television through a national closed circuit over the Columbia Broadcasting System to carry to its members and their colleagues a SYMPOSIUM ON THE MANAGEMENT OF HYPERTENSION. This telecast is made possible through the cooperation and generous support of Wyeth Incorporated of Philadelphia, and will be the *first nationwide* closed circuit hookup for postgraduate medical education.

The panel of distinguished physicians who will participate includes:

Cyrus C. Sturgis, M.D., F.A.C.P., Presiding President, American College of Physicians, Professor of Internal Medicine, University of Michigan, Ann Arbor.

F. H. Smirk, M.D., F.R.A.C.P., Professor of Medicine, University of Otago, Dunedin, New Zealand.

Garfield G. Duncan, M.D., F.A.C.P., Director of the Medical Division, Pennsylvania Hospital, Philadelphia.

R. W. Wilkins, M.D., F.A.C.P., Chief, Hypertension Clinic, Massachusetts Memorial Hospital, Boston.

Edward D. Freis, M.D. (Associate), Adjunct Clinical Professor of Medicine, Georgetown University, Washington.

Professor Smirk is one of the topmost authorities of the world on methonium compounds. He went to New Zealand from England in 1940 to take the Chair of Medicine at the University of Otago. He is a Fellow of the Royal College of Physicians of London and of the Royal Australasian College of Physicians, being the Senior Censor for the latter in New Zealand. He appears on this program as an official representative of the Royal Australasian College of Physicians in connection with an exchange-guest program being arranged between the two colleges.

A "closed TV circuit" is one by which reception is controlled and not open to the general TV public. This telecast cannot be picked up in the home, but the invited audience must go to the TV receiving station. Twenty-three such receiving stations will be used; these will be located in Boston, New York, Philadelphia, Washington, Pittsburgh, Charlotte, Atlanta, Cincinnati, Detroit, Chicago, St. Louis, Milwaukee, Minneapolis, Memphis, Dallas, Houston, New Orleans, Denver, Salt Lake City, Los Angeles, San Francisco, Baltimore and Cleveland.

CITE RECOVERY IN CARDIAC ARREST WITH LEVOPHED INJECTION IN HEART

Wickenburg, Ariz.—In a procedure never before attempted, the vasoconstrictor Levophed was injected directly into a human heart "dead" nearly five minutes, causing the heart to resume beating immediately, according to Drs. Frederick A. Shannon and William N. Henry.

Reporting in *Arizona Medicine* (July 1954) they state the patient recovered completely and had returned to work as a truck driver about six weeks after the ordeal. Follow-up observation failed to reveal any damage to the brain or other organs, or any bizarre behavior. The doctors emphasize the significance of these findings in light of statements elsewhere in medical literature that the brain cannot survive more than three minutes after the heart stops beating, without suffering irreversible damage.

The patient in the Arizona study, a 26-year-old man, was operated on for an inflamed appendix. While in the process of closing the incision, the heart and respiration suddenly stopped. Forced respiration was begun and was continued throughout the procedure.

About three minutes after cardiac arrest had occurred, the patient's chest was opened and the heart massaged. At this point, the authors write, cardiac massage was momentarily discontinued to permit a comparatively massive dose of Levophed, one cc. of a 4:1000 solution, to be injected directly into the right ventricle. Following the injection, a total of about four minutes and forty-five seconds having elapsed, fibrillation ensued but was immediately replaced by a rapid shallow heart rate estimated at 160.

When massage was resumed, the rate slowed down to 120, with much greater cardiac output. Massage was slowly discontinued about five minutes after the heart stopped beating, with the blood pressure in the next ten minutes reaching 124/90, and the pulse less than 100. Voluntary respiration, which had ceased, was also resumed, at first in a shallow and incomplete manner.

Two previous cases of cardiac arrest under surgery attended by Dr. Henry prompted the decision to attempt, for the first time, an injection of Levophed into the heart. In both earlier instances, however, he reports that a smaller dose was administered, and by vein. The pa-

tients eventually died, although the hearts resumed beating for from two to six hours.

"Experience with these two cases led to the conclusion that if any measure of success was to be attained by the use of Levophed, the solution would have to be administered in greater concentration and more rapidly," the Arizona surgeons say.

However, in a patient adequately atropinized, they suggest the dose of Levophed to be one-third to one-half of the one cc. concentration used in their emergency case. The latter is believed to have been "poorly atropinized."

In view of the doubtful results obtained with epinephrine, intracardiac injections of Levophed are recommended in its place.

INTERNATIONAL ACADEMY OF PROCTOLOGY

The International Academy of Proctology announces the establishment of a Teaching and Research Fellowship in proctology under the direction of Dr. Marcus D. Kogel, Dean of the newly formed Albert Einstein College of Medicine, New York City. The Academy has voted a $1,000 Annual Grant for each of three years to assist in the development of research and educational projects in proctology at the University.

One of the suggested projects is the establishment of a pathological tissue slide "library" for teaching purposes, under the direction of Dr. Alfred Angrist, Professor of Pathology.

As emphasized by the founder and Secretary of the International Academy of Proctology, Dr. Alfred J. Cantor, Flushing, New York, at the time of the Sixth Annual Convention of the Academy in Chicago, the major function of the Academy is educational. All Academy funds are to be used for research and teaching projects in proctology so that earlier diagnosis and better treatment of patients with diseases of the colon and rectum may be made universally available.

The Academy offers a Teaching Seminar, open to all physicians without fee, each year. Research Fellowships in proctology are sponsored by the Academy, and three such Fellowships were voted at the time of the last Annual Meeting. Dr. Earl J. Halligan, Director of Surgery of the Jersey City Medical Center, and International Secretary-General of the Academy, is in charge of a Research Fellowship at the Jersey City Medical Center. Additional Fellowships were voted to be established in the Mid-west and on the West Coast of the United States.

FIND ASPIRIN AS EFFECTIVE AS CORTISONE IN ARTHRITIS

The ordinary aspirin tablet is just as effective as the hormone cortisone in the treatment of early cases of rheumatoid arthritis, according to a report published in the *British Medical Journal* (1:1223, May 29, 1954).

Findings of clinical trials with 61 patients were released by a joint committee of the British Medical Research Council and Nuffield Foundation, following one year's treatment with the two agents.

"For practical purposes, there appears to have been surprisingly little to choose between cortisone and aspirin in the management of these 61 patients in the early stages of rheumatoid arthritis," the committee states.

Only minor side effects were caused by each drug, although fewer patients receiving aspirin experienced reactions as the study progressed.

Patients with a disease duration of three to nine months only were selected for the comparative study. While not too severely crippled by the disease, they were required to have had at least four affected joints. The test cases were admitted to six different arthritis centers in England. Cortisone was given to 30 patients and aspirin to 31. To prevent recognition, the aspirin was administered in brown tablets and given a bitter taste.

Treatment lasted over a period of one year, consisting of 12-week courses separated by one-week without treatment. The article notes that results were determined on the basis of the return of general functional capacity; elimination of tenderness in inflamed joints; restoration of range of movement; return of strength in grip; and improved manual dexterity.

"Observations made one week, eight weeks, 13 weeks and approximately one year after the start of treatment reveal that the two groups ran a closely parallel course in nearly all the recorded characteristics."

Three-fourths in each group were virtually free of pain and disability at the end of a year, and almost half were able to go back to work, the study found.

NEW OINTMENT, WHICH USES ZIRCONIUM, INTRODUCED FOR PREVENTION AND TREATMENT OF POISON IVY

A new ointment has been introduced by Parke, Davis & Company for the prevention and treatment of poison ivy and poison oak.

Called Ziradryl Cream, it makes use of the metal zirconium to neutralize the poisonous effect of ivy and oak.

Ziradryl Cream combines hydrated zirconium carbonate with Benadryl hydrochloride in a water-miscible base.

"This offers the chemical neutralizing action of zirconium and the antihistaminic benefits of Benadryl for topical application," the firm explained.

Parke-Davis said Ziradryl Cream helps protect against the dermatitis (inflamed skin) resulting from exposure to poison ivy and oak if applied before contact with the plants or as soon as possible after contact.

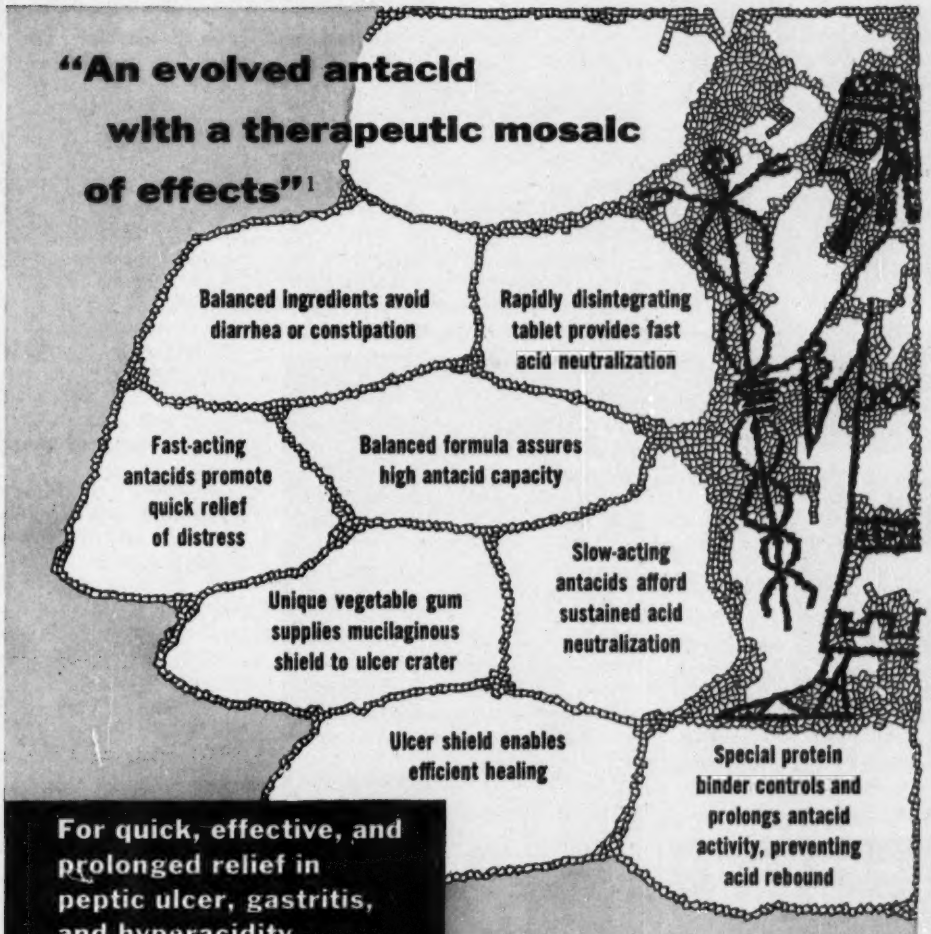
The new product also helps decrease the acute dermatitis occurring in those persons susceptible to the irritating action of the two plants.

Urushiol (an orthodihydroxybenzene derivative) is the toxic agent in poison ivy and, in contact with zirconium, combines to form a non-irritating salt.

In one clinical study, 47 patients were treated with a zirconium preparation for dermatitis following exposure to ivy poisoning. Within 24 hours after beginning treatment, 39 showed relief from the itching, and inflammation had subsided.

Another medical report found that hydrous zirconium oxide prevented appearance of dermatitis from poison ivy when applied to the skin of susceptible subjects within one hour after exposure to urushiol.

Two physicians used a cream containing zirconium and an antihistamine to treat army personnel about to enter an area having a heavy



For quick, effective, and prolonged relief in peptic ulcer, gastritis, and hyperacidity . . .

prescribe TREVIDAL®

Trevidal is available in boxes of 100 tablets, specially stripped for easy carrying.

IN EACH TABLET:

Aluminum hydroxide gel, dried	90 mg.
Calcium carbonate	105 mg.
Magnesium trisilicate	150 mg.
Magnesium carbonate	60 mg.
Egraine*†	45 mg.
Regonol*‡	100 mg.

*Trade Mark †Protein binder from oat ‡Cyamopsis tetragonoloba gum

[1]C. B. DeCourcy, and C. Rhomberg, Staff. Conf. DeCourcy Clinic, 26, June 15, 1954

Organon INC. · ORANGE, N. J.

growth of poison oak. Three hundred and twenty-three soldiers were instructed to apply the cream on exposed areas on entering the field, on arising daily and after washing. A second group of 228 used a placebo cream, and an additional 355 received no medication.

Of those treated with the zirconium-antihistamine cream, only 9.6 per cent showed signs of dermatitis, while the incidence of poison oak in the other groups was 21.9 per cent and 20.6 per cent, respectively.

A recent pharmaceutical survey showed more than an 8 per cent rise in the sale of products to treat poison ivy last year, and a similar increase is predicted this year.

Ziradryl Cream is supplied in one-ounce tubes.

INFANTILE PARALYSIS

The National Foundation for Infantile Paralysis has announced the award of grants and appropriations totaling $2,486,244, effective July 1, for research and professional education in poliomyelitis and related fields. Grants went to 30 different medical schools, universities, hospitals, research institutions and educational organizations in the U. S. and two in other countries.

Of the total sums authorized, $1,506,148 were granted for research in virology and epidemiology and in prevention and treatment of after-effects of poliomyelitis and related conditions, and $980,096 in grants and appropriations were allocated for programs of professional education.

These new awards bring to a total of $74,000,000 the money provided in March of Dimes funds since 1938 for research in virology and epidemiology, prevention and treatment of after-effects of poliomyelitis, clinical studies of medical care problems, polio prevention and aid to professional and public education. In addition, from 1938 up to this year, the National Foundation has expended an additional $174,700,000 in meeting costs of treatment for patients needing help.

Among the lines of research that will receive new and increased emphasis as a result of the National Foundation grants are: lysogenesis or the phenomena associated with dormant viruses or pro-viruses; tissue culture techniques and applications, especially the search for stable strains of normal mammalian cells that can be propagated indefinitely *in vitro;* the development of a practical complement fixation test for the early diagnosis of poliomyelitis; and study of the chemical structure of the nucleic acids and other components of virus particles.

The National Foundation grants for professional education are designed to increase the pool of qualified professional workers needed for the total care, meaning rehabilitation, of patients handicapped by poliomyelitis and other diseases. These grants supply and augment educational opportunities for physicians, undergraduate medical students and associate medical personnel, including nurses, physical therapists, occupational therapists, and medical social workers.

EVERYBODY EATS BUT MOTHER

America's homemakers are so busy taking care of their family's needs that they often neglect their own meals.

The diets of women over 30 are deficient in milk, foods that contain Vitamin C like citrus fruits, and vegetables, according to a research report by Dr. Elizabeth Wiegand of the New York State College of Home Economics at Cornell University.

Forty per cent of the women in the 30 to 90-year age group are overweight. Deficient diets not only affect the physical health of homemakers, the report points out, but manifest themselves in irritability, pessimism, nervousness and fatigue. (Source: New York Times, Apr. 25, 1954.)

TERIDAX PRODUCES EXCELLENT GALLBLADDER VISUALIZATION IN CLINICALLY STUDIED SERIES OF PATIENTS

Excellent visualization of the gallbladder with notable freedom from side effects has been obtained in 66 out of a series of 90 cases with Teridax, according to a report by Dr. C. Rowell Hoffmann in the June issue of the *American Journal of Digestive Diseases.* Teridax is a product of Schering Corporation, Bloomfield, N. J. pharmaceutical manufacturers.

According to Dr. Hoffmann, the density of the Teridax cholecystograms was measured photometrically and found to be between that of two other media, a characteristic which he stated was highly desirable, since excessive density has been found to mask the presence of stones. The shadow produced by Teridax was sufficiently dense to visualize the gall-bladder fluoroscopically in every case, the author reported.

Twenty-six of the patients studied had active peptic ulcers. Teridax proved to be nonirritating to any of these patients.

In five patients studied at 2 hour intervals for 18 hours, the gallbladder was faintly discernible at 4 hours and visible at six. Sufficient dye remained in the gallbladder to permit critical studies for a period of 8 to 18 hours.

The cystic and common ducts, and occasionally the hepatic ducts, were well visualized with Teridax when the fatty meal was employed.

Dr. Hoffmann concluded from the results of his studies that (1) Teridax rarely produces unabsorbed radiopaque material in the

colon, and if present, the colonic opacities in no way confuse cholecystographic interpretation; (2) the density of the radiographs obtained with Teridax are in an ideal opacity range, permitting better visualization of gravel-type stones than the more dense medium, which at times may completely mask them; and (3) "Teridax has resulted in a lower incidence of discomforting side actions than has any other cholecystographic medium employed to date."

FURACIN

In a report on approximately 400 cases of urethritis treated with Furacin® urethral suppositories, Dr. Vernon H. Youngblood, Cabarrus Memorial Hospital, Concord, N. C., noted symptomatic improvement "as early as 1 day after beginning treatment." He added that "the average period of treatment is 13 days." His results are reported in the Journal of Urology (*70*:926 (Dec.) 1953).

Dr. Youngblood found that the use of Furacin suppositories "requires a minimum of office visits, does away with the pain of urethral dilatations and silver nitrate applications. . . . The patient can easily use the medication at home herself."

The suppositories contain Furacin 0.2 per cent with the topical anesthetic diperodon hydrochloride 2 per cent in a water dispersible base.

PARKE-DAVIS ANNOUNCES NEW PRODUCT TO AID IN BLASTOMYCOSIS DIAGNOSIS

Parke, Davis & Company has announced a new product, Blastomycin, for use in the skin-test diagnosis of Blastomycosis, also known as Gilchrist's Disease.

Blastomycosis is a fungus infection which may occur in any part of the body, but particularly attacks the skin, lungs and bones, resulting in lesions (unhealing sores).

The new Parke-Davis product is the sterile filtrate from a culture of Blastomyces dermatitidis and is standardized according to the National Institutes of Health regulations.

The skin test was devised to aid in the diagnosis of Blastomycosis because the disease is similar to certain forms of tuberculosis, syphilis, certain fungus-type infections, and a number of other conditions.

The recommended test dosage is prepared by diluting the vial of concentrated Blastomycin (.01 cc.) with 1.0 cc. of diluent. In performing the test, the company said, 0.1 cc. of the diluted Blastomycin is injected intracutaneously into the forearm of the patient and the reaction is read 24 to 48 hours later.

Parke-Davis advises that the tuberculin and Histoplasmin test should be employed in conjunction with the Blastomycin in order to exclude the possibility of tuberculosis and histoplasmosis.

Blastomycin is supplied as two 1-cc. vials, one containing .01 cc. of concentrated Blastomycin and the other containing 1 cc. of diluent.

Once the material, which is available only on prescriptions, has been diluted it may be kept for 30 days at refrigerator temperature without loss of potency.

ROBITUSSIN

To determine the effect of Robitussin (Robins) in allergic and

infectious bronchial asthma, the A. H. Robins Co., Inc., Richmond, Va., has made a grant to Dr. Emanuel Schwartz, assistant professor of medicine and chief of the allergy clinic at Long Island College Hospital, Brooklyn, N. Y. Dr. Schwartz will study control of cough in approximately 100 seasonal and nonseasonal cases. The study will last a year.

BLASTOMYCIN

What the Product Is—A sterile filtrate from the culture of the mycelial phase of Blastomyces dermatitidis grown on liquid synthetic medium.

What It's For—An aid in the diagnosis of North American Blastomycosis (Gilchrist's Disease) and the differentiation from other infections.

How Supplied—In two 1-cc. vials, one containing .01 cc. of Blastomycin and the other containing 1 cc. of diluent.

Who Supplies It—Parke, Davis & Company.

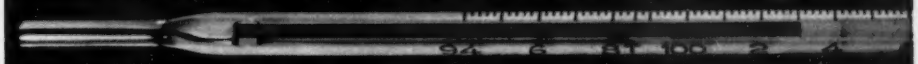
NEW CONCENTRATED BACTINE OFFERED TO PROFESSION

Concentrated BACTINE,® a new economical space-saving form of BACTINE the widely used germicide, fungicide and deodorizer, has been offered for professional use as announced by Miles Laboratries, Inc., Elkhart, Indiana.

The concentrated form is eight times as strong as the standard BACTINE. It is packaged in individually cartoned pint bottles with one dozen in a shipping case. When diluted with water, each pint makes one gallon of the standard preparation. A convenient sprayer bottle is currently provided to professional people at no extra cost.

BACTINE contains a quaternary ammonium compound reinforced by other active components with specific functions and therefore has qualities in addition to those associated with quaternaries. For example, besides being an excellent germicide, it has considerable fungicidal, topical anesthetic and antipruritic actions. It has been employed by physicians, nurses, dentists, hospitals, chiropodists and veterinarians.

WHEN TETRACYN THERAPY IS INDICATED



AND THE PATIENT CANNOT OR WILL NOT

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FOR AN **AIH** (AFEBRILE IN HOURS) RESPONSE

NEW DOSAGE FORM

- affords prompt control in a wide range of infections
- provides a convenient route of administration for "stat" therapy
- keeps control of therapy in the hands of the physician

SUPPLIED: Vials of 100 mg.

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chocolate flavored

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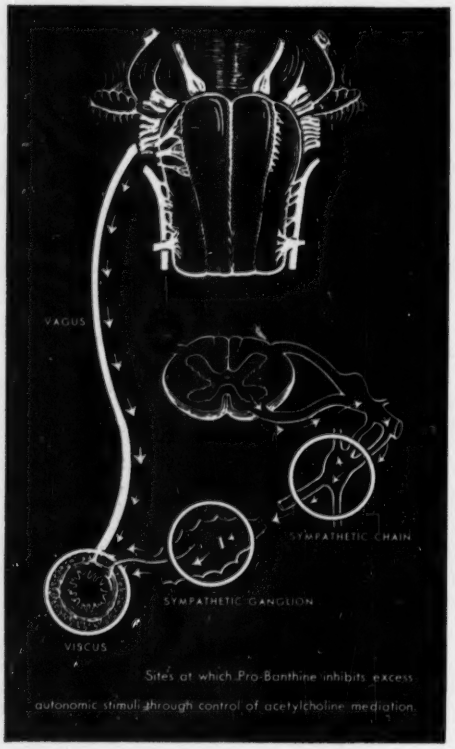
Pro-Banthine®: For Anticholinergic Action in the Gastrointestinal Tract

Combined neuro-effector and ganglion inhibiting action of Pro-Banthine consistently controls gastrointestinal hypermotility and spasm and the attendant symptoms.

Pro-Banthine is an improved anticholinergic compound. Its unique pharmacologic properties are a decided advance in the control of the most common symptoms of smooth muscle spasm in all segments of the gastrointestinal tract.

By controlling excess motility of the gastrointestinal tract, Pro-Banthine has found wide use[1] in the treatment of peptic ulcer, functional diarrheas, regional enteritis and ulcerative colitis. It is also valuable in the treatment of pylorospasm and spasm of the sphincter of Oddi.



Sites at which Pro-Banthine inhibits excess autonomic stimuli through control of acetylcholine mediation.

Roback and Beal[2] found that Pro-Banthine orally was an "inhibitor of spontaneous and histamine-stimulated gastric secretion" which "resulted in marked and prolonged inhibition of the motility of the stomach, jejunum, and colon. . . ."

Therapy with Pro-Banthine is remarkably free from reactions associated with parasympathetic inhibition. Dryness of the mouth and blurred vision are much less common with Pro-Banthine than with other potent anticholinergic agents.

In Roback and Beal's[2] series "Side effects were almost entirely absent in single doses of 30 or 40 mg. . . ."

Pro-Banthine (β-diisopropylaminoethyl xanthene-9-carboxylate methobromide, brand of propantheline bromide) is available in three dosage forms: sugar-coated tablets of 15 mg.; sugar-coated tablets of 15 mg. of Pro-Banthine with 15 mg. of phenobarbital, for use when anxiety and tension are complicating factors; ampuls of 30 mg., for more rapid effects and in instances when oral medication is impractical or impossible.

For the average patient one tablet of Pro-Banthine (15 mg.) with each meal and two tablets (30 mg.) at bedtime will be adequate. G. D. Searle & Co., Research in the Service of Medicine.

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1. Schwartz I. R.; Lehman, E.; Ostrove, R., and Seibel, J. M.: Gastroenterology *25*:416 (Nov.) 1953.

2. Roback, R. A., and Beal, J. M.: Gastroenterology *25*:24 (Sept.) 1953.